temperature) by a broad resonance at 2.65 ppm, which separates into two resonances (2.69 ppm and 2.55 ppm) at −16 °C and sharpens to a single resonance (2.64 ppm) at 40 °C. Photolysis of **3** in methylcyclohexane at −196 °C (glass matrix) and −78 °C to 25 °C (solution) using a Hanovia high-pressure lamp (quartz) produced no apparent change as monitored by ^{1}H NMR at the corresponding temperatures (−78 °C and 25 °C, respectively).

We believe the model that best describes bonding interactions in **3** is, at least at −25 °C, that of a π-complex, a formulation which has been developed for three-membered ring Main Group heterocycles.[8,9] Further experimental and theoretical investigations are currently underway to probe this model for stannacyclopropenes.

Acknowledgment. We thank Kimberly Orsborn for her assistance in preparing **2**, Dr. Robert Donohoe for collection of the Raman data, Dr. Cynthia Day of Crystalytics Co. for the structural analysis of **3**, and CMU for a Faculty Development Grant.

Supplementary Material Available: Detailed information concerning the spectral data and crystallographic analysis of **3**, including listings of atomic coordinates and temperature factors, bond lengths, bond angles, anisotropic temperature factors, and an ORTEP representation of **3** (11 pages). Ordering information is given on any current masthead page.

(8) (a) Dewar, M. J. S. *Bull. Soc. Chim.* **1951**, *18*, C71. (b) Hoffmann, R.; Fujimoto, H.; Swenson, J. R.; Wan, C.-C. *J. Am. Chem. Soc.* **1973**, *95*, 7044. (c) Dewar, M. J. S.; Ford, G. P. *J. Am. Chem. Soc.* **1979**, *101*, 783. (d) Cremer, D.; Kraka, E. *J. Am. Chem. Soc.* **1985**, *107*, 3800.

(9) This model is, in essence, identical with that for the Dewar–Chatt–Duncanson description of transition-metal olefin and acetylene complexes, see: (a) Dewar, M. J. S. *Bull. Soc. Chim.* **1951**, *18*, C79. (b) Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939.

A New Strategy for 1,4- and 1,4,7-Polycarbonyl Compounds

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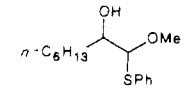
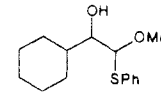
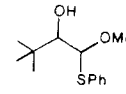
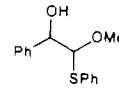
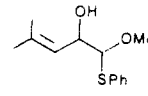
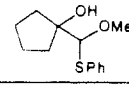
1,4-Dicarbonyl compounds constitute key intermediates in various natural product syntheses, and a number of methodologies for their syntheses have appeared.[1] Now we report a conceptually new strategy based on the successive C_1 and C_2 homologation of an aldehyde which can be extended to the synthesis of 1,4,7-tricarbonyl compounds.

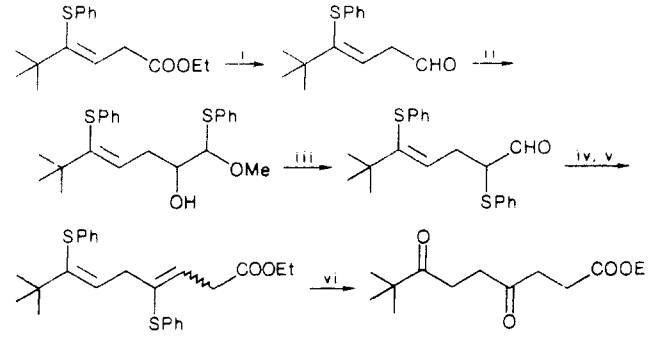
In the course of the studies on synthetic applications of methoxy(phenylthio)methane (**1**),[2] we have found that exposure of the carbonyl adducts **2**[3] to methanesulfonyl chloride–triethylamine provides α-sulfenyl aldehydes **3** in good yields (eq 1, Table I).[4] Previously de Groot et al. reported analogous phenylthio migration reaction with thionyl chloride–pyridine which,

Table I. Synthesis of α-Phenylthioaldehydes **3**[a]

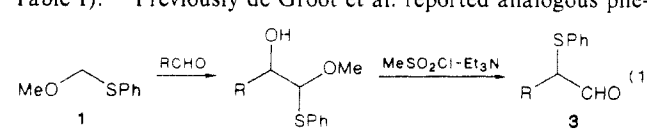
entry	**2**	$MeSO_2Cl$ (equiv)	Et_3N (equiv)	reactn time, h	**3** yield,[b] %
1		1.5	1.5	12	83
2		1.3	1.3	12	79
3		1.8	1.8	12	88
4		1.3	1.3	0.25[c]	77
5		1.3	1.3	1[c]	71
6		3.3	3.3	24	88

[a] Reaction conditions: in benzene at 20 °C unless otherwise noted. [b] Isolated yields after column chromatography. All compounds gave satisfactory NMR, IR, and HRMS spectral data. [c] In benzene–hexane (4:1) at 0 °C.

Scheme I[a]



[a] (i) DIBAH (1.0 equiv), toluene, −78 °C, 15 min; (ii) MeO(PhS)CHLi (3 equiv), THF, −78 to −40 °C, 1 h, 51% through i and ii; (iii) $MeSO_2Cl$ (1.5 equiv)–Et_3N (1.5 equiv), benzene, 0 °C, 1 h, 68%; (iv) **6a** (2.0 equiv), THF, 50 °C, 12 h; (v) *t*-BuOK (1.6 equiv), THF, −78 °C, 30 min, 75% through iv and v; (vi) CF_3COOH–H_2O (4:1), 20 °C, 10 h, 100%.



nylthio migration reaction with thionyl chloride–pyridine which,

(1) Reviews: Ellison, R. A. *Synthesis* **1973**, 397. Ho, T.-L. *Synth. Commun.* **1974**, *4*, 265. Rio, G.; Lecas-Nawracka, A. *Bull. Soc. Chim. Fr.* **1976**, 317. 1,4-Addition of acyl anion or its equivalent to α,β-unsaturated systems: Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* **1969**, *91*, 4926. Seyferth, D.; Hui, R. C. *J. Am. Chem. Soc.* **1985**, *107*, 4551. Shono, T.; Nishiguchi, I.; Ohmizu, H. *J. Am. Chem. Soc.* **1977**, *99*, 7396. Scheffold, R.; Orlinski, R. *J. Am. Chem. Soc.* **1983**, *105*, 7200. Mukaiyama, T.; Narasaka, K.; Furusato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641. Stork, G.; Maldonado, L. *J. Am. Chem. Soc.* **1974**, *96*, 5272. Albright, J. D. *Tetrahedron* **1983**, *39*, 3207. Groebel, B.-T.; Seebach, D. *Synthesis* **1977**, 357. Stetter, H. *Angew. Chem.* **1976**, *88*, 695. Krief, A. *Tetrahedron* **1980**, *36*, 2531. Acylation of homoenolate anions: Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397. Ponaras, A. A. *Tetrahedron Lett.* **1976**, 3015. Hosomi, A.; Hashimoto, H.; Sakurai, H. *J. Org. Chem.* **1978**, *43*, 2551. Ryu, I.; Matsumoto, K.; Ando, M.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1980**, *21*, 4283. Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 3368. Coupling of acyl and β-oxo radicals: Wehrli, P.; Chu, V. *J. Org. Chem.* **1973**, *38*, 3436. Cerfontain, H.; van Noort, P. C. M. *Synthesis* **1980**, 490. Coupling of enolates: Crombie, L.; Harper, S. H. *J. Chem. Soc.* **1952**, 869. Miyashita, M.; Yanami, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1976**, *98*, 4679. Kosugi, M.; Takano, I.; Sakurai, M.; Sano, H.; Migita, T. *Chem. Lett.* **1984**, 1221. Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 4605. Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487. For other methods: Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205.

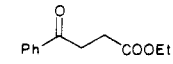
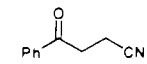
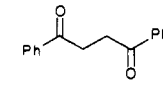
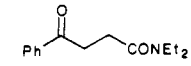
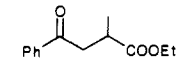
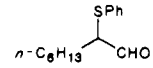
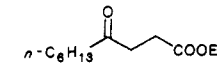
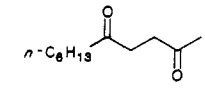
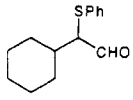
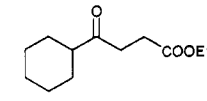
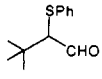
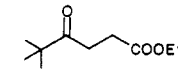
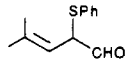
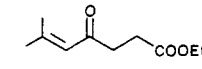
(2) For the previous study of this series: Sato, T.; Okura, S.; Otera, J., Nozaki, H. *Tetrahedron Lett.* **1987**, *28*, 6299. For a review: Otera, J. *Synthesis* **1988**, 95.

(3) Mandai, T.; Hara, K.; Nakajima, T.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1983**, *24*, 4993.

(4) α-Phenylthiobutyraldehyde was obtained in 45% yield by tosylation of the corresponding adduct: Rawal, V. H.; Akiba, M.; Cava, M. P. *Synth. Commun.* **1984**, *14*, 1129.

0002-7863/88/1510-5209$01.50/0

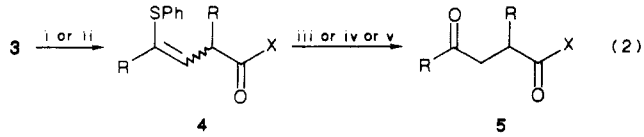
Table II. Synthesis of 1,4-Dicarbonyl Compounds **5**

entry	3	6 or 7[a] (equiv)	reactn time,[b] h	*t*-BuOK (equiv)	reactn time,[b] h	% yield of 4[c] (*E*/*Z*)[d]	reactn condn[e]			5[c]	yield, %
								temp, °C	time, h		
1	 **3a**	**6a** (2)	1	*f*		87 (1/3)	A	20	3		94
2	**3a**	**7a** (1.3)	2	*f*		74 (1/3)	B	0–20	3		46
3	**3a**	**6b** (1.5)	1	*f*		60 (1/9)	A	20	5.5		71
4	**3a**	**6c** (2)	10	*f*		61 (1/4)	B	20	120		74 (100)[g]
5	**3a**	**6d** (1.5)	14	1.6	1	66 (1/6)	C	65	72		74
6	 **3b**	**7b** (1.3)	1	1.3	1	63 (1/1)	C	65	14		82
7	**3b**	**7c** (1.3)	0.25	2	0.5	51 (1/1)	B	20	6		91
8		**7b** (1.3)	0.5	1.3	0.5	55 (3/7)	A	20	2.5		79
9		**6a** (2)	12	1.6	0.5	85 (0/10)	A	20	10.5		82
10		**6a** (2)	1	1.5	0.5	80 (1/1)	B	−20	0.3		68

[a] **6a**, $Ph_3P{=}CHCOOEt$; **6b**, $Ph_3P{=}CHCOPh$; **6c**, $Ph_3P{=}CHCONEt_2$; **6d**, $Ph_3P{=}C(Me)COOEt$; **7a**, $(EtO)_2P(O)CH(Na)CN$; **7b**, $(EtO)_2P(O)CH(Na)COOEt$; **7c**, $(EtO)_2P(O)CH(Na)COMe$. [b] In THF. [c] All compounds gave satisfactory NMR, IR, and HRMS spectral data. [d] Determined on the basis of NMR spectra. [e] A, CF_3COOH–H_2O (4:1)/CH_2Cl_2; B, CF_3COOH–H_2O (4:1); C, concentrated H_2SO_4/95% EtOH. [f] **4** was obtained without the base treatment. [g] A portion of **4** was recovered. The yield based on the consumed **4** is given in the parentheses.

however, was not effective for adducts with aldehydes.[5,6] In contrast to extensively investigated α-sulfenylated ketones and esters,[7] the aldehyde analogues have found rather limited applications due to the lack of an efficient preparative method.[5,7,8]

With the general, simple method for **3** in hand, we started to develop a new strategy leading to 1,4-dicarbonyl compounds (eq 2). Exposure of **3** to the Wittig (or Wittig–Horner) reagent and



(2)

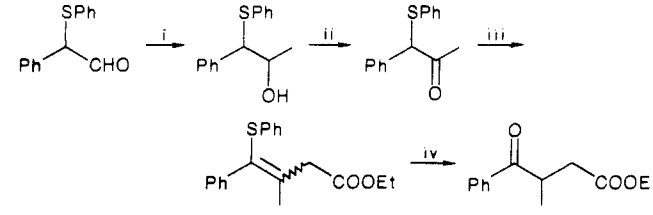
4 **5**

X = OR, NR_2, R, Ph, etc.

(i) $Ph_3P{=}CRCOX$ (**6**), THF, 50 °C; (ii) $(EtO)_2P(O)CR(Na)COX$ (**7**), THF, 0 °C, then *t*-BuOK, THF, −78 °C; (iii) CF_3COOH–H_2O (4:1), CH_2Cl_2; (iv) CF_3COOH–H_2O, (v) concentrated H_2SO_4, 95% EtOH.

the *t*-BuOK-promoted isomerization of the resulting α,β-unsaturated compounds provided γ-phenylthio-β,γ-unsaturated carbonyl compounds **4**.[9] Conversion of the vinyl sulfide moiety into the carbonyl function led to the desired 1,4-dicarbonyl compounds **5** (Table II). Versatility of this procedure is evident from the applicability to γ-oxo esters, nitriles, amides, and ketones including 2,5-undecadione, the precursor of dihydro jasmone (entry 7).[1] None of the precedent procedures can satisfy such a broad spectrum of functionality.

The generality is further shown by the following example. The



(i) MeMgBr, THF, 0 °C, 70%; (ii) Me_2SO (1.3 equiv), $(COCl)_2$ (2.6 equiv), Et_3N (5.0 equiv), CH_2Cl_2, −50 to −20 °C, 1 h, 64%; (iii) $(EtO)_2P(O)CH(Na)COOEt$ (2.5 equiv), 20 °C, 12 h, 45%; (iv) CF_3COOH–H_2O (4:1), CH_2Cl_2, 20 °C, 48 h, 62%.

methyl group of the Grignard reagent was incorporated at the β-carbon of the resulting ester. Accordingly, appropriate choice of the Wittig and Grignard reagents enables us to conduct sub-

(5) de Groot, Ae.; Jansen, B. J. M. *Tetrahedron Lett.* **1981**, 887.
(6) For phenylthio migration of β-hydroxy sulfides, see: Warren, S. *Acc. Chem. Res.* **1978**, *11*, 401.
(7) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363. Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453.
(8) Bestmann, H. J.; Angerer, J. *Liebigs Ann. Chem.* **1974**, 2085. Coates, R.; Pigott, H.; Ollinger, J. *Tetrahedron Lett.* **1974**, 3955. Seebach, D.; Teschner, M. *Chem. Ber.* **1976**, *109*, 1601. Brownbridge, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1131 and 2272. Groenewegen, P.; Kallenberg, H.; van der Gen, A. *Tetrahedron Lett.* **1979**, 2817. Duhamel, L.; Chauvin, J.; Messier, A. J. *Tetrahedron Lett.* **1980**, *21*, 4171. Duhamel, L.; Chauvin, J.; Messier, A. J. *J. Chem. Res.* [*S*] **1982**, 48. Verhe, R.; De Kimpe, N.; De Buyck, L.; Schamp, N. *Synthesis* **1984**, 46. de Groot, Ae.; Jansen, B. J. M. *Synthesis* **1985**, 434. Shimagaki, M.; Takubo, H.; Oishi, T. *Tetrahedron Lett.* **1985**, *26*, 6235. Aggarwal, V. K.; Warren, S. *Tetrahedron Lett.* **1986**, *27*, 101.

(9) In some cases, the isomerization occurred in situ in the first step (see entries 1–4 in Table II). The base-promoted isomerization of γ-phenylthio-α,β-unsaturated esters into the β,γ-unsaturated compounds has been reported: Brownbridge, P.; Hunt, P. G.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 3391. Brownbridge, P.; Durman, J.; Hunt, P. G.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1947.

stitution on either of the α and β-positions.

Of particular significance is that our procedure renders the carbonyl functions under protection as alkenyl thioethers until the final stage, allowing further C_3 homologation. Indeed, the synthesis of one 4,7-diketoester was achieved as illustrated in Scheme I.[10]

We suppose that the repeated $C_1 + C_2$ elongation will proceed without difficulty to provide higher homologs. Therefore, the strategy disclosed herein is promising and practical to afford polycarbonyl compounds bearing the repeating β-carbonyl C_3 units.

Acknowledgment. This work was supported in part by Grant-in-Aid for Scientific Research on Priority Area, "Advanced Molecular Conversion", The Ministry of Education, Science, and Culture, Japan.

Supplementary Material Available: NMR and spectral data for compounds in this paper (8 pages). Ordering information is given on any current masthead page.

(10) For recent syntheses of 1,4,7-triketones see: Stetter, H.; Basse, W.; Kuhlmann, H.; Landscheidt, A.; Schlenker, W. *Chem. Ber.* **1977**, *110*, 1007. Stetter, H.; Landscheidt, A. *Chem. Ber.* **1979**, *112*, 1410 and 2419. Ryu, I.; Ryang, M.; Rhee, I.; Omura, H.; Murai, S.; Sonoda, N. *Synth. Commun.* **1984**, *14*, 1175.

Molecular Yardsticks. Synthesis of Extended Equilibrium Transfer Alkylating Cross-link Reagents and Their Use in the Formation of Macrocycles

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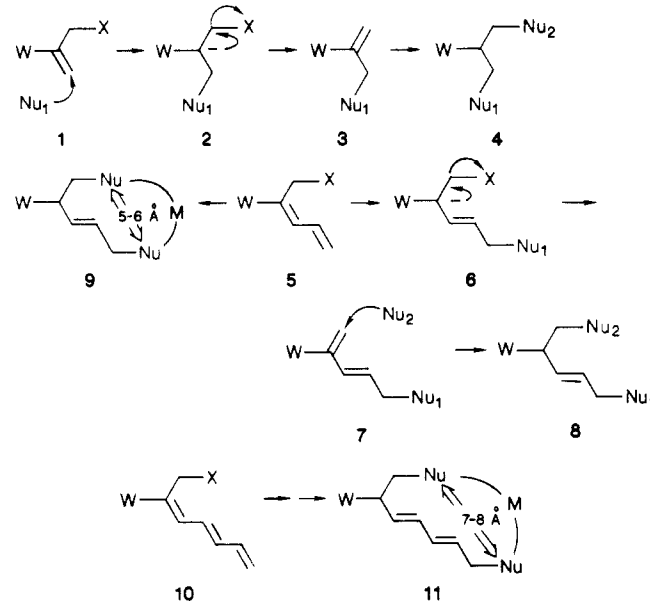
Some years ago our group introduced reagents [**1**] for sequential alkylation through consecutive Michael reactions [**1** → **4**].[1] Since that time, a variety of different Michael activating groups [W = $-CO_2R$, -COR, $-NO_2$, -CN, $-SO_2-R$, $O_2N-C_6H_4-$] and leaving groups [X = -Cl, -Br, $-N(CH_3)_3^+$, $-OCOC(CH_3)_3$] have been explored for this sequence of reactions. Seebach and Knochel,[2] Stetter,[3] Cromwell,[4] Doomes,[5] Fuchs,[6] Peters and van Bekkem,[7] and others have made beautiful contributions to this chemistry. The technique was extended by us to the cross-linking of proteins.[8] We have sought an efficient entry to structurally and mechanistically similar molecules having high Michael reactivity, suppressed direct displacement chemistry, and extended conjugation [for example **5** or **10**]. The extended structures are "yardsticks", able to bridge incrementally longer distances between nucleophilic

Scheme I



groups in either complex proteins or simple frameworks. This cross-linking concept can be extrapolated to the chemical synthesis of interesting macrocyclic rings [**9** and **11**].

The competition between direct displacement and Michael addition in the first step of the sequence depends upon the attacking nucleophile [Nu1], activation [W] of the double bond, and character of the leaving group [X]. Keto hydroxyethylsulfonylmethyldiene and polyene structures [**12–21**, Scheme II] were chosen as meeting the desired criteria. Such molecules contain an α-methylene with a leaving group (X = SO_2-R) not prone to direct displacement combined with a strong activating group for the Michael reaction (W = ketone) that could be easily reduced in aqueous media. This last criterion was required so that in protein systems the equilibrium transfer process can be arrested if necessary and the linked sites can be identified.[8] The hydroxyl group was appended to give a chelating arm for synthetic reasons and for providing attachment sites for water solubilizing groups in protein cross-link studies. The nitro function was appended to give a site for eventual attachment of probes for protein studies. Various degrees of conjugation [**12**, **18**, **21**] and of double bond substitution [**13–17**, **18–20**] were prepared to determine their effects on the primary site of Michael addition.[9] These molecules are constructed in a remarkably efficient way by a chelated titanium-mediated aldol–dehydration sequence.

Adding $TiCl_4$ and diisopropylethylamine[10,11] at −40 °C to β-((2-hydroxyethyl)thio)-*m*-nitropropiophenone [**30**], mp 58.0–58.5 °C (prepared from the corresponding Mannich salt[12]), in THF gave a chelated complex **31** which condensed with aldehydes[13] giving essentially quantitative yields of the hydroxyethylthiomethylenones [**32**, R = H, CH_3, C_6H_5, $CH{=}CH_2$, $CH{=}CH$-C_6H_5, etc.] with a 10–15:1 *Z*/*E* selectivity of the major isomer as determined by NMR analysis of the crude product mixture. Oxidation of the olefinic sulfides by *m*-CPBA in chloroform at 0 °C for 5 min gave the corresponding sulfones in good isolated yields (60–90%). The stereochemistry about the newly formed double bonds for these ((2-hydroxyethyl)sulfonyl)methyl dienes, trienes, and tetraenones [**12–21**] has been substantiated to be of

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