Tetrahedron. Vol. 25, pp. 3675 to 3679. Pergamon Press 1969. Printed in Great Britain

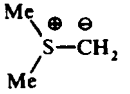
REACTIONS OF CARBONYL-STABILIZED SULPHONIUM YLIDES WITH GRIGNARD REAGENTS

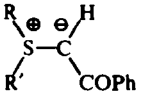
H. NOZAKI, K. NAKAMURA and M. TAKAKU
Department of Industrial Chemistry, Kyôto University, Kyôto, Japan

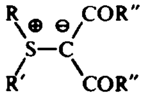
(*Received in Japan* 5 *February* 1969; *Received in the U.K. for publication* 17 *March* 1969)

Abstract—Sulphonium diacylmethylides $RR'\overset{\oplus}{S}—\overset{\ominus}{C}(COR'')_2$ react with $R'''MgX$ to afford ketones $R''COR'''$, if either R'' or R''' has an α-hydrogen. In the absence of this, for example, the reaction of $R(Me)\overset{\oplus}{S}—\overset{\ominus}{C}(COPh)_2$ with PhMgBr results in elimination of the S-Me and gives a product RS—$C(COPh_2$. If R, R′, R″ and R‴ are all Ph groups, benzophenone and $Ph_2\overset{\oplus}{S}—\overset{\ominus}{C}HCOPh$ are formed. The reaction of phenacylides $R(Me)\overset{\oplus}{S}—\overset{\ominus}{C}HCOPh$ with R‴MgX proceeds with elimination of R‴Me to produce $RSCH_2COPh$. Reactions of PhLi with these ylides are also recorded.

ACYL-SUBSTITUTION at the ylide carbon increases the thermal stability of sulphonium ylides and decreases the nucleophilic reactivity. Thermally labile dimethylsulphonium methylide (I)[1] reacts with certain olefins to afford cyclopropanes and reacts with carbonyl compounds to produce oxiranes. In contrast phenacylides IIa[2] and IIb[3],


I


IIa: R = R′ = Me
IIb: R = Me, R′ = Ph
IIc: R = R′ = Ph


IIIa: R = R′ = Me, R″ = Ph
IIIb: R = Me, R′ = R″ = Ph
IIIc: R = R′ = R″ = Ph
IIId: R = R′ = R″ = Me

which are stable to isolation and react smoothly with electrophilic olefins but only sluggishly with carbonyl compounds. Doubly acylated methylides III are completely devoid of such nucleophilic reactivity. Reactions of extremely stabilized ylides III of this kind, with organometallic reagents have been investigated in order to find novel Grignard reactions as formulated below.*

Benzoylation of ylides IIa, IIb and IIc[5] gave IIIa[2], IIIb[3] and IIIc, respectively, whereas condensation of dimethyl sulphoxide and acetylacetone furnished IIId[6].

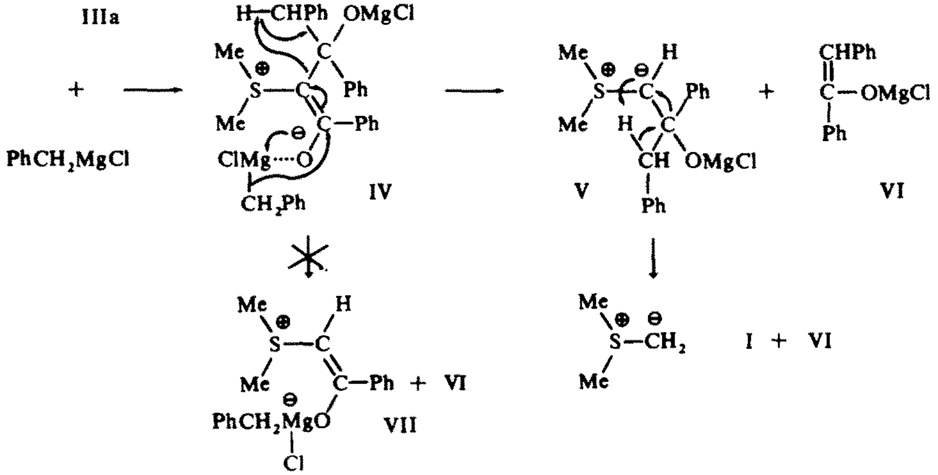
The ylide IIIa was treated with two mole equivalents of $PhCH_2MgCl$ in boiling THF solution. Work up gave desoxybenzoin in an 84% yield or 168 mole % based on IIIa. In contrast, the reaction of IIId gave very inferior yields of ketones. The action of $PhCH_2MgCl$ or of PhMgBr under similar conditions gave benzyl methyl ketone (34%) and acetophenone (25%), respectively, along with a very complex mixture of byproducts which were not characterized. The anomalously high yield of desoxybenzoin

---

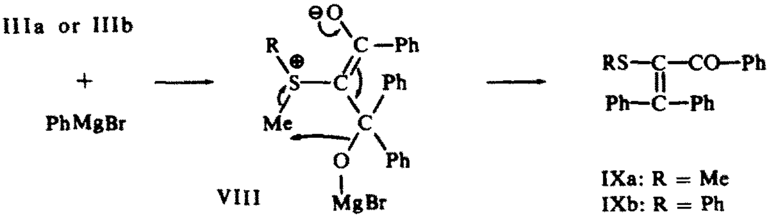
* For the Grignard reaction of phosphonium compounds, see Ref. 4.

naturally requires a mechanism, in which both benzoyl groups of IIIa are detached from the ylide carbon. A tentative account for this is represented in Scheme A. The 1:2 adduct IV would probably experience both elimination of an enolate VI and the second carbonyl attack concertedly to form V, which eliminates a molecule of the enolate VI to produce methylide I. The fate of I has not been clarified, as no product arising therefrom has been isolated. Another possible route of IV to VII appears to be unwarranted, since the reaction VII has been established to proceed in a different way as described below. If the postutlation of the Scheme A is correct, the absence of hydrogen to be captured by the ylide carbon would give rise to other reactions than the one yielding the enolates. Actually, treatment of ylides IIIa or IIIb with PhMgBr was shown to afford enones IXa (79%) and IXb (77%), respectively, under elimination of the S–Me group from the possible adducts VIII (Scheme B). The spectral data of enones IXa and IXb are consistent with the structures given. Desulphurization of IXa with Raney nickel gave β, β-diphenylpropiophenone, whereas IXb gave a mixture of the saturated ketone and β,β-diphenylacrylophenone.

SCHEME A



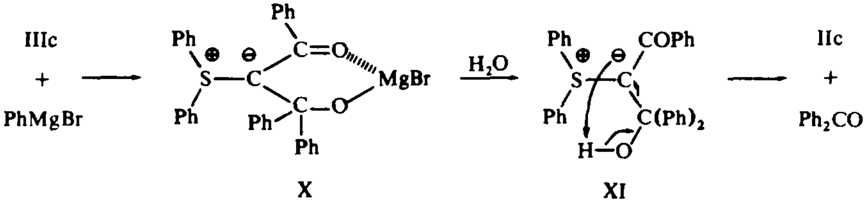
SCHEME B



Diphenylsulphonium dibenzoylmethylide (IIIc) was synthesized by the reaction of diphenylsulphonium phenacylide (IIc)[5] with benzoic anhydride in the presence of triethylamine. The reaction of IIIc with phenylmagnesium bromide was found to afford IIc (42%) and benzophenone (79%). A possible scheme for these products is as follows. The primary adduct X is stable and survives in contrast to VIII and the free acid XI produced on work up decomposes to give IIc and benzophenone (Scheme C).

In order to examine the fate of the Grignard adduct VII, the ylides IIa and IIb were treated with Grignard reagents. Reaction of IIa with $PhCH_2MgCl$ afforded α-(methylthio)acetophenone (26%) and *trans*-1,2,3-tribenzoylcyclopropane (1%). Either $PhMgBr$ or $PhCH_2MgCl$ reacted with IIb to give mainly the same product, α-(phenylthio)acetophenone, in 59% and 57% yields respectively. The removal of S-Me group would presumably proceed *via* the adduct VII under elimination of R—Me. Diphenylsulphonium phenacylide (IIc) reacted with PhMgBr to produce *trans*-1,2,3-tribenzoyl cyclopropane in a 90% yield. No carbonyl addition products were isolated in these reactions.

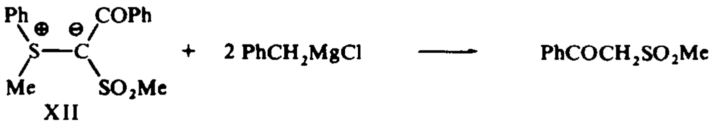
SCHEME C



Organolithium compounds behaved similarly towards these ylides. The reaction of PhLi with IIId gave acetophenone in a 34% yield.The ylide IIIa reactedwith PhLi to afford IXa in a 27% yield besides benzophenone in a 45% yield. The formation of benzophenone is unexpected and remains unexplained. Conceivably, the adduct corresponding to VIII is stable and in this case gives benzophenone on work up (Scheme C). The complex nature of byproducts did not allow further detailed analysis of the products. The reaction of ylide IIb with PhLi gave α-(phenylthio)acetophenone in a 60% yield.

Finally, the fourth type of reaction (Scheme D) was observed with a ketosulphone ylide XII.[7] Treatment with $PhCH_2MgCl$ gave α-(methanesulphonyl)acetophenone (68%) as a main product. The Grignard reagent would probably behave as a hydrogen source in this reaction but its further fate is still obscure. Treatment of XII with PhMgBr gave an extremely complex mixture which could not be identified. The nature of these reactions is open to research in the future.

SCHEME D



EXPERIMENTAL

All m.ps and b.ps are uncorrected. Microanalyses were performed at the Elemental Analyses Centre of Kyôto University. The NMR spectra were obtained on JEOL C-60-H spectrometer.

Grignard reagents were prepared as usual and standardized according to the method of Gilman.[8] An ethereal soln of PhLi was prepared and standardized by the method of Gilman.[9]

Reaction of IIIa *with benzylmagnesium chloride as a general procedure of the reactions of ylides with Grignard reagents.* A soln of $PhCH_2MgCl$ (35·2 mmoles) in THF (40 ml) was added dropwise over a period of 1 hr to a stirred soln of IIIa (5·0 g, 17·6 mmoles) in THF (10 ml) under reflux in an atm of N_2. After the addition was complete, the reaction mixture was stirred for 1 hr at the same temp and then cooled at 0°. To this mixture was added dropwise, saturated NH_4Cl aq over a period of 30 min. The contents were stirred at room temp for 1 hr and then extracted with $CHCl_3$ (300 ml). The extract was washed with water, dried ($MgSO_4$) and concentrated. Most of the residual oil was solidified on cooling in a Dry Ice–MeOH bath. The solid was triturated with pet ether (b.p. 30–50°) and filtered. The filtrate was concentrated and the residual oil was chromatographed on a column of Florisil (30 g) with hexane-benzene as an eluant to yield 1·9 g of the same crystals as above in addition to small amounts of $PhCH_2OH$ and $(PhCH_2)_2$. The combined crystals (6·1 g) were recrystallized from MeOH to give desoxybenzoin (5·8 g, 84%), m.p. and mixed m.p. 60°. The identity was further confirmed by IR spectrum.

Preparation of α-methylthio-β,β-diphenylacrylophenone (IXa) *and α-phenylthio-β,β-diphenylacrylophenone* (IXb). The reaction of ylide IIIa (5·0 g, 17·6 mmoles) with PhMgBr (35·2 mmoles) afforded 4·6 g (79%) of IXa, m.p. 123–124° (from PhH-hexane). NMR: δ ($CHCl_3$) 2·12 (3H, s), 7·0–8·2 (15H, m). IR (KBr): 1656, 1240 cm^{-1}; UV: λ_{max}^{EtOH} 251 nm (log ε 4·38). (Found: C, 80·3; H, 5·6. $C_{22}H_{18}OS$ requires: C, 80·0; H, 5·5%).

Analogously the reaction of IIIb with PhMgBr gave IXb (77%), m.p. 123–124° (from PhH-hexane). NMR: δ($CHCl_3$) 7·0–8·2 (m). IR (KBr): 1650, 1243 cm^{-1}. UV: λ_{max}^{EtOH} 254 nm (log ε 4·42). (Found: C, 82·6; H, 5·1. $C_{27}H_{20}OS$ requires: C, 82·6; H, 5·1%). Mixed m.p. of IXa and IXb was 92–95°.

Desulphurization of IXa *and* IXb. Raney Ni catalyst (W-2, 25 g) was added in one portion to a soln of IXa (2.0 g, 6·1 mmoles) in acetone (30 ml). The mixture was then heated at reflux for 3 hr, filtered, and the filtrate was concentrated. Recrystallization of the residue from EtOH afforded β,β-diphenylpropiophenone (1·2 g, 69%), m.p. 93–94° (lit.[10] 94–95°); NMR δ($CHCl_3$) 3·72 (2H, d), 4·85 (1H, t), 7·0–8·0 (15H, m); IR (KBr): 1678, 1212 cm^{-1}. (Found: C, 87·8; H, 6·2. Calc. for $C_{21}H_{18}O$: C, 88·1; H, 6·3%). Analogously IXb was desulphurized to afford β,β-diphenylpropiophenone (9·7%) and β,β-diphenylacrylophenone (88%), m.p. 85·5–86·5° (lit.[10] 86–87°). NMR: δ($CHCl_3$) 7·13 (1H, s), 7·15–8·10 (15H, m). IR (KBr): 1657, 1206 cm^{-1}. (Found: C, 88·8; H, 5·9. Calc. for $C_{21}H_{16}O$: C, 88·7; H, 5·7%).

Preparation of diphenylsulphonium dibenzoylmethylide (IIIc). A soln of IIc[5] (3·0 g, 9·9 mmoles), Et_3N (1·0 g, 9·9 mmoles), and benzoic anhydride (2·3 g, 10 mmoles) in THF (350 ml) was heated at reflux for 3 days. After cooling the reaction mixture was diluted with water (300 ml) and extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and evaporated. The residual solid was recrystallized from benzene to give colourless crystals of IIIc (1·4 g, 35%), m.p. 186–187°; IR (KBr): 1540, 1325 cm^{-1}. NMR: δ($CHCl_3$) 7·0–7·9 (m). (Found: C, 79·7; H, 5·2. $C_{27}H_{20}O_2S$ requires: C, 79·4; H, 4·9%).

Reaction of IIIc *with phenylmagnesium bromide.* The ylide IIIc (3·0 g, 7·4 mmoles) was allowed to react with PhMgBr (14·8 mmoles) in THF to yield IIc (0·94 g, 42%), BzPh (1·05 g, 7·9%), Ph_2S (0·59 g, 43%) and *trans*-1,2,3-tribenzoylcyclopropane, m.p. and mixed m.p. 213–214°[11], (0·04 g, 5%).

Reaction of IIb *with phenylmagnesium bromide.* Reaction of IIb (5·0 g, 21 mmoles) with PhMgBr (21 mmoles) afforded α-(phenylthio)acetophenone (2·8 g, 59%), *trans*-1,2,3-tribenzoylcyclopropane (0·30 g, 12%) and PhSMe (0·73 g, 29%).

Reaction of XII *with benzylmagnesium chloride.* Treatment of XII (2·0 g, 6·3 mmoles) with $PhCH_2MgCl$ (12·5 mmoles) in THF gave an oil, which was chromatographed on a column of Florisil. Elution with benzene and ether afforded α-(methanesulphonyl)acetophenone (0·84 g, 68%), m.p. 105–106° (lit.[12] 110°). (Found: C, 54·8; H, 5·0. Calc. for $C_9H_{10}O_3S$: C, 54·5; H, 5·1%).

Reaction of IIIa *with phenyllithium as a general procedure of the reaction of ylides with phenyllithium.* A soln of PhLi (71 mmoles) in ether (72 ml) was added to a suspension of IIIa (10·0 g, 35 mmoles) in ether (20 ml) at room temp under N_2 over 1 hr. The mixture was stirred for an additional 22 hr at the same temp and then treated with sat NH_4Cl aq. This mixture was diluted with water and extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed on a column of Florisil (30 g) with PhH-hexane to yield BzPh (5·8 g, 45% or 90 mole%) and IXa (3·1 g, 27% or 27 mole%).

Acknowledgements—The authors are indebted to Professor K. Sisido for help and encouragement. They are grateful to Dr. K. Kondô for valuable discussion. This work was partially supported by the Scientific Research Fund of Ministry of Education, Japanese Government.

REFERENCES

[1] E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.* **87**, 1353 (1965).

[2] [a] A. W. Johnson and R. T. Amel, *Tetrahedron Letters* 819 (1966);
[b] K. W. Ratts and A. N. Yao, *J. Org. Chem.* **31**, 1185 (1966);
[c] B. M. Trost, *J. Am. Chem. Soc.* **89**, 138 (1967).

[3] H. Nozaki, M. Takaku and K. Kondô, *Tetrahedron* **22**, 2145 (1966).

[4] T. Mukaiyama, I. Kuwajima and R. Yoda, *Abstracts of Papers* Presented at the 21st Annual Meeting of the Chemical Society of Japan, No. 4118 (1968).

[5] T. Hashimoto, H. Yano, H. Kitano and K. Fukui, *Nippon Kagaku Zasshi* **89**, 703 (1968).

[6] [a] H. Nozaki, Z. Morita and K. Kondô, *Tetrahedron Letters* 2913 (1966);
[b] R. Oda and Y. Hayashi, *Nippon Kagaku Zasshi* **87**, 1110 (1966).

[7] H. Nozaki, M. Takaku, Y. Hayasi and K. Kondô, *Tetrahedron* **24**, 6563 (1968).

[8] H. Gilman, E. A. Zoellner and J. B. Dickey, *J. Am. Chem. Soc.* **51**, 1576 (1929).

[9] R. G. Jones and H. Gilman, *Organic Reactions* Vol. **6**, p. 353 Wiley, New York (1951).

[10] K. H. Meyer and K. Schuster, *Chem. Ber.* **55**, 819 (1922).

[11] G. Maier, *Ibid.* **95**, 611 (1962).

[12] H. Böhme, R. Frank and W. Krause, *Ibid.* **82**, 433 (1949).