**S-[3-Cyano-2-oxo-3-(triphenyl-λ^5-phosphanylidene)propyl] O-ethyl Carbonodithioate: A Novel Xanthate Reagent for the Synthesis of α-keto (cyanomethylene)triphenylphosphorane Ylides from Olefins**

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Since the first report of phosphorane ylide-based synthetic route for α-keto amide/ester units by Wasserman’s group in 1994, it has widely been used in the synthesis of numerous complex compounds including peptides due to its mild reaction conditions and outstanding convergence. This route, however, has the limitation that α-keto (cyanomethylene)-triphenylphosphorane ylides 2, the key intermediates in Wasserman’s route, can be prepared only from carboxylic acids or acid chlorides (Scheme 1).

In a series of papers recently published by us, we have developed new synthetic approaches to α-keto cyanophosphorane ylides from readily available chemicals using specially designed new reagents to overcome such limitation. For example, α-keto cyanophosphorane ylides have been prepared from carbonyl compounds using a new Horner-Wadsworth-Emmons (HWE) reagent, from alkyl bromides using a new phenylsulfonil reagent via sequential alkylation-reductive desulfonation protocol.

In continuation of our interest in this field of chemistry, we envision that a novel xanthate reagent 4 having α-oxo cyanophosphorane subunit could undergo group transfer addition to olefins 5 under radical conditions and subsequent reduction of 6 would afford α-keto cyanophosphorane ylides 2' in a concise manner (Scheme 2).

The realization of the new synthetic approach requires the successful synthesis of requisite xanthate 4, which has been prepared from the intermediate 8 and potassium O-ethyl xanthate in acetone in 95% yield as a stable solid (Scheme 3).

**Scheme 1.** Wasserman's synthetic route for α-keto amide/ester units.

**Scheme 2.** A plausible synthetic approach to α-keto cyanophosphorane ylides 2' from olefins utilizing a novel xanthate reagent 4 (where Xa = -SC(=S)OEt).
The formation of 2'a appears to be surprising, however, it could be rationalized that as xanthate addition to 5a proceeds, undecyl radical derived from DLP attacks the xanthate group in 6a to form 2'a. In this reduction, 1-octene itself may work as a hydrogen atom donor presumably by allylic hydrogen in 1-octene. Interestingly this type of concomitant xanthate addition/partial xanthate reduction continued throughout the olefins reacted. The concomitant xanthate addition/complete xanthate reduction was reported in the case of 2'-oxaoxalkyl xanthate addition to olefins with (EtO)2P=O)/DLP. Upon increasing the amount of 5a to (2.5 eq & 3.0 eq), the combined yields of (6a/2'a) were gradually improved to 82% and 84% respectively (run 2, 3). Thus the conditions of (run 3) were adopted as the standard conditions.

In order to examine the tolerance of widely used functionalities in organic synthesis, various olefins substituted with diverse functionality were reacted with 4 under the standard conditions. Simple aryl olefin 5b and olefins with ketone, ester, nitrite, or carbonate have shown similar reactivity towards 4 affording (6c-g/2'c-g) in good to excellent combined yields (67-83%) (run 5-9). Allyl benzyl ether (5h), however, gave a moderate yield (58%) of (6h/2'h) probably due to the benzyl subunit (run 10). In overall, representative functionalities widely used in organic synthesis are proven to be stable enough under these radical conditions.

We next turned our attention to xanthate reduction in 6. Due to high toxicity, cost and separation problem associated with Bu3SnH7 we decided to use DLP/2-propanol8 and H3PO4/Et3N/AIBN8 as tin-free procedures, and the representative results are summarized in Table 2.

For the reductive removal of xanthate group in 6 with DLP/IPA, 6 were heated at reflux in i-propyl alcohol (IPA) with excess of DLP (2.2 eq) for 2 h under Ar. The procedure proceeded well for 6a-g affording 2'a-g in 57-87% yields (run 1-7). However, 6h gave a moderate yield (42%) of 2'h along with several by-products probably due to the benzylic hydrogen that can be easily abstracted by radical (run 8). Presumably high radical concentration due to excess of DLP might hamper the desired reduction and bring forth severe side reactions. We then attempted H3PO4/Et3N/AIBN in 1,4-dioxane under reflux conditions. This reduction protocol necessitated catalytic amount of AIBN (0.6 eq) as a radical initiator, which in turn might reduce side reactions caused by radical, thereby increasing the yields of 2'. In fact, the yields of 2' were improved considerably compared to DLP/IPA method in most cases.

In conclusion, a new synthetic approach to α-keto cyano phosphorane ylides from olefins utilizing a novel xanthate reagent 6 has been developed. There are several advantages expected from this new approach e.g., easy preparation of 6 from commercial reagents in excellent yield, mild reaction conditions, good to excellent overall yields. Currently we are doing additional experiments to determine the scope and limitation of this new approach, and those results will be reported in due course.

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References and Notes

4. Analytical data of xanthate reagent 4: Yield: 95%; A white solid; mp 169-170 °C; IR (KBr) 2178, 1594 cm\(^{-1}\); 1H NMR (CDCl3, 400 MHz) \(\delta\) 1.39 (t, J = 7.1 Hz, 3H), 4.39 (s, 2H) 4.62 eq. J = 7.1 Hz, 2H), 7.48-7.68 (m, 15H); 13C NMR (CDCl3, 100 MHz) \(\delta\) 13.72, 43.37, 43.45, 48.24, 49.50, 70.09, 122.14, 123.07, 129.11, 129.24, 133.24, 133.26, 133.58, 133.68, 187.85, 187.89, 213.90; MS (AP/Cl) \(m/z\) 464 [M+H]+; Anal. calcd. for C28H20NO3PS: C, 64.78; H, 4.78; N, 3.02; found: C, 64.72; H, 4.80; N, 3.03.
5. Analytical data of xanthate adduct 6a & reduced adduct 2’a: \(R_1 = 0.65 (\text{CH}_3\text{Cl}/\text{EtOAc}, 40/1)\); A colorless liquid; IR (KBr) 2174, 1587 cm\(^{-1}\); 1H NMR (CDCl3, 400 MHz) \(\delta\) 0.86 (t, 3 H, J = 6.8 Hz), 1.17-1.49 (m, 11H), 1.60-1.77 (m, 2H), 1.87-2.01 (m, 1H), 2.03-2.12 (m, 1H), 2.78-2.92 (m, 2H), 2.92-2.95 (m, 1H), 4.64 (qd, 2H, \(J_1 = 7.1\) Hz, \(J_2 = 3.2\) Hz), 7.47-7.67 (m, 15H); 13C NMR (CDCl3, 100 MHz) \(\delta\) 13.77, 14.03, 22.55, 26.63, 29.14, 29.30, 31.65, 34.37, 36.80, 36.87, 47.60, 48.86, 51.23, 69.06, 122.35, 125.50, 128.81, 129.04, 129.16, 133.02, 133.04, 133.51, 133.57, 136.32, 195.72, 195.77, 214.82; MS (AP/Cl) \(m/z\) 576 [M+H]+; Anal. calcd. for C38H28NO3PS: C, 68.84; H, 6.65; N, 2.43; found: C, 69.03; H, 6.64; N, 2.33; \(R_1 = 0.44 (\text{CH}_3\text{Cl}/\text{EtOAc}, 40/1)\); a white solid; mp 115-116 °C (lit\(^b\) 116-117 °C); IR (KBr) 2173, 1582 cm\(^{-1}\); 1H NMR (CDCl3, 400 MHz) \(\delta\) 0.88 (t, 3 H, J = 6.8 Hz), 1.17-1.39 (m, 12H), 1.57-1.72 (m, 2H), 2.68 (t, 2H, J = 7.6 Hz), 7.47-7.66 (m, 15H).