ACETONITRILE: AN EXCELLENT SOLVENT FOR THE 1,1-DICHLOROMETHYLENATION OF CERTAIN KETONES

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Abstract: Cyclohexanones react rapidly at or below room temperature with Ph_3P and XCCl₃ (X=Br or Cl) in acetonitrile to give 1,1-dichloromethylene compounds in high yield; some α -methoxyimino β -(1,1-dichloro)methylene esters have been similarly prepared.

We recently wished to prepare the alcohol (1) as a synthetic intermediate; the known ketone $(2)^1$ seemed an obvious precursor. However, reaction of this material under standard conditions (Ph₃P, excess CCl₄, reflux) gave the mono-chloro olefin (3) in moderate yield plus unreacted ketone, in keeping with the reported behaviour of cyclohexanone itself.²



Various other conditions for the transformation (2) (4) were possible,³ but these involved more complex reagents or critical control of reaction conditions. Thus by using (dichloromethyl)triphenylphosponium chloride (5)⁴ a 57% yield of (4) was obtainable [2eq. (5), 2eq. NaH in THF, leq. (2), 1.5h at reflux]. We investigated the effect of solvent on the simple Ph₃P/CCl₄ reaction, reasoning from the behaviour of other cyclic ketones that only slight differences in solvation or stabilisation of intermediates might divert the reaction from production of (3) to (4).

$$[Ph_{3}PCHCl_{2}]Cl^{-} Ph_{3}P=CCl_{2} \longleftrightarrow Ph_{3}P-CCl_{2}$$
(5)
(6)

Our results are summarised in Table 1. The choice of acetonitrile was based on a review by Appel⁵ where it was pointed out that acetonitrile can have a marked accelerating effect on Ph_3P/CCl_4 reactions, owing to its high dielectric constant and solvating ability compared to CCl_4 itself. We expected that acetonitrile could give good stabilisation of the ylid (6) and thus aid our desired transformation. While the use of Ph_3P (2eq.)/CCl₄



(leq.) gave a mixture of (3) and (4), it will be seen that with Ph_3P (4eq.)/CCl₄(2eq.) an excellent yield of highly pure (4)⁶ was obtained, under mild conditions. The replacement of CCl₄ by BrCCl₃⁷ is also noteworthy, giving an even faster and higher-yielding reaction (final entry). The simpler derivatives cyclohexanone (7) and 4-methylcyclohexanone (8) similarly afforded respectively (9) (93%) and (10) (90%) (after chromatography) from the $Ph_3P/CCl_4/MeCN$ conditions. Thus the use of acetonitrile both directs the reaction mixture to the desired product and achieves a large rate acceleration.

Solvent	Reagents/conditions	Products	
cc1 ₄	Ph3P (leq.), △, 16H	(3) 51% + (2) 30%	
THF	Ph ₃ P (2eq.), CCl ₄ (leq.) \triangle , 16h	(3) 78% + (2) ca. 10%	
MeCN	Ph ₃ P (2eq.), CC1 ₄ (1eq.), 20°C, 16h	(4) 60% + (3) 32%	
MeCN	Ph ₃ P (4eq.), CCl ₄ (2eq.), 20°C, 2h	(4) 91% + (3) < 5% (n.m.r.)	
MeCN	Ph3P (4eq.), BrCCl3 (2eq.), 20°C, 1h	(4) 100%	

Table 1. Reaction of Ketone (2) with Ph3P/CCl4 under various conditions.

We have further investigated the use of these conditions in another reaction of interest to us, namely the conversion of the α -methoxyimino β -ketoesters (lla-c) to the corresponding l,l-dichloromethylene compounds (l2a-c) (Table 2).



b : $R = CF_3$, $R^1 = Et$ c : $R = MeOCH_2$, $R^1 = Me$

(11a-c)

∮ ÔMe OR1

о́Ме

Although in this series MeCN has a less dramatic effect, our conditions still offer clear advantages, namely mildness, faster rate and avoidance of side reactions. The further advantage offered by BrCCl₃ is evident from the second and third entries. It should be noted that, in the third column, prolonged reflux in CCl₄ is necessary (5-10h) and much dark, tarry material is produced, making product isolation tedious.

		Method/yield of (12a→c)		
Subtrate	Product	Ph ₃ P, Xs CC1 ₄ Δ	Ph ₃ P (4eq.)/CCl ₄ (2eq.), MeCN, 20°C	Ph ₃ P (3eq.)/BrCC1 ₃ (1.5eq.), MeCN, 0 →20°C
(11a)	(12a)	41% ⁸	94% ⁹	-
(115) ¹⁰	(12Ъ)	55%	61%	80%
$(11c)^{10}$	(12c)	44%	67%	71%

Table 2. Preparation of (α -methoxyimino β -dichloromethylene) esters.

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<u>Procedure</u>: 4-Methylcyclohexanone (0.56g, 5mmol) was stirred with triphenylphosphine (5.24g, 20mmol) in anhydrous acetonitrile (10ml) under argon at 0°C. Carbon tetrachloride (1.54g, 10mmol) was added in one portion and the mixture was allowed to regain room temperature. Stirring was continued until no triphenylphosphine was visible by t.l.c. (usually about 2h). The solution was diluted with ether, washed with water (2x), brine, dried and evaporated to dryness. Flash silica gel chromatography gave 4-methyl-(1,l-dichloro)methylenecyclohexane (0.80g, 90%). An analytical sample was obtained by Kugelrohr distillation. Found: Cl, 39.6%; <u>M</u>, 178.0322. C₈H₁₂Cl₂ requires Cl, 39.7%; M, 178.0317.

References and Notes

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- Compound (4) and other new compounds described gave satisfactory analytical and spectroscopic data, by Kugelrohr distillation in the case of (10).
- 7. B.A. Clement and R.L. Soulen, J. Org. Chem., 1976,41, 556.
- 8. From E (lla); we also obtained



- 9. From <u>Z</u> (11a).
- 10. Both starting material and product thought to be single E-isomers.

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