A Novel Reduction of Activated Olefins by Lithium Amides

By **Uri Melamed** and **Ben-Ami Feit**,* Department of Chemistry, Tel-Aviv University, Tel Aviv, Israel

Activated olefins of the type $Ph_2C=CXY$ (X and Y being electronegative substituents) reacted in tetrahydrofuran a low temperature with lithium amides having a hydrogen atom at C-α, to give the corresponding saturated derivatives. The reduction took place by a transfer of a hydride ion from the amide to the activated double bond.

VINYL carbanions derived from activated olefins of the type $\begin{array}{c}\diagup\\\diagdown\end{array}C=C\begin{array}{c}\diagup H\\\diagdown A\end{a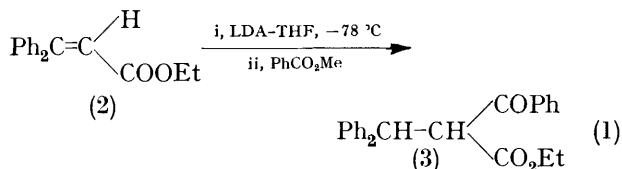rray}$ (A = CN, CO_2R, *etc.*) are intermediates of great interest and importance due to their potential application as nucleophiles in organic synthesis. A few studies of this type have been recently reported.[1,2,3] Some complications have already been encountered [4] which require further study of the reactions taking place between activated olefins and different bases in the absence of any added electrophile. Knowledge of the factors affecting these reactions will make possible the proper application of vinyl carbanions as nucleophiles.

$Ph_2C=CH-A$ were not reduced. In the case of olefin (5) two additional products were obtained. Reduction occurred only with amides having an H atom on C-α and not for example with lithium 2,2,6,6-tetramethyl-piperidide (LTMP).
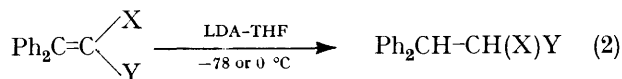
Olefin (1) could be obtained by using LTMP instead of LDA under the conditions of equation (1). The yields of the reduced olefins were about the same in THF and in diethyl ether, indicating that the reduction reaction was not dependent on the nature of the N^-Li^+ and the C^-Li^+ ion-pairs. Organolithium compounds exist in diethyl ether as 'intimate' ion-pairs which are much less reactive than the solvent-separated ion-pairs

existing in the THF.[5] The results are summarized in the Table.
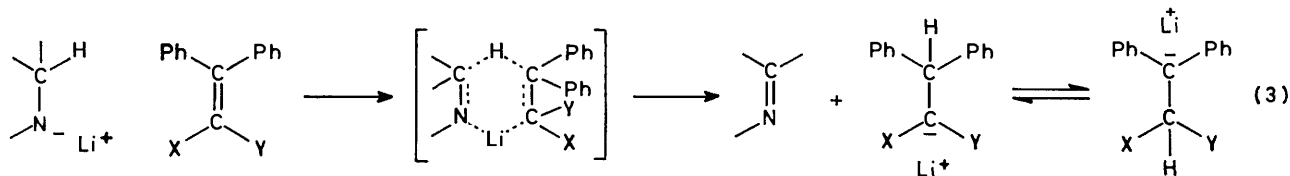
The olefinic β-keto-ester $Ph_2C=C(COPh)CO_2Et$ (1) was the expected product of the reaction of the vinyl carbanion derived from $\beta\beta$-diphenylacrylate (2) with methyl benzoate, but the saturated derivative (3) was the one obtained [equation (1)]. On using benzophenone and

$$Ph_2C=C\begin{array}{c}\diagup H\\\diagdown COOEt\end{array} \xrightarrow[\text{ii, PhCO}_2\text{Me}]{\text{i, LDA-THF, } -78\ ^\circ\text{C}}$$
(2)

$$Ph_2CH-CH\begin{array}{c}\diagup COPh\\\diagdown CO_2Et\end{array} \quad (1)$$
(3)

benzaldehyde as electrophiles in the presence of lithium di-isopropylamide (LDA), diphenylmethanol, and benzyl alcohol, respectively, were the by-products obtained. It was found in the present work that $\beta\beta$-diphenyl-activated olefins reacted with LDA and with lithium bicyclo-hexylamide (LBCA) in THF and in ether to give the corresponding saturated derivatives [equation (2)].

$$Ph_2C=C\begin{array}{c}\diagup X\\\diagdown Y\end{array} \xrightarrow[-78\text{ or }0\ ^\circ\text{C}]{\text{LDA-THF}} Ph_2CH-CH(X)Y \quad (2)$$
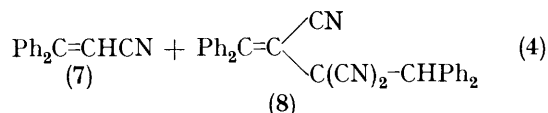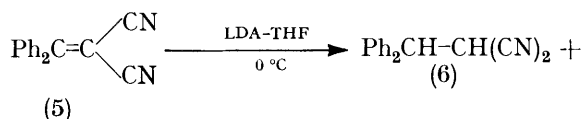
(1) X = CO_2 Et, Y=COPh
(4) X = CO_2 Et, Y = CN
(5) X = CN, Y = CN

Olefins having two electronegative substituents [(1), (4), and (5)] were easily reduced whereas olefins of the type

Based on the experimental results we suggest the following mechanism for the presently studied reduction [equation (3)]. The first step consists of a hydride transfer from the lithium amide to the activated olefin *via* a cyclic transition state. A free hydride ion is not involved in the reaction under the experimental conditions employed. The resulting carbanion rearranges to the relatively more stable carbanion. The intense colouration of the reaction mixture observed is due to the presence of the conjugated carbanions. Because of the small size of the nucleophile, steric hindrance does not prevent the attachment of H^- to C-β, which is the normal site of nucleophilic attack on an activated olefin. The nucleophilic attack of bulkier nucleophiles such as butyl-lithium and sodium ethoxide on $\beta\beta$-diphenyl-acrylonitrile [4] and on $\beta\beta$-diphenylfluoroethylene,[6] respectively, took place at C-α.

The products formed in the case of the LDA–olefin (5) reaction system strongly support the proposed mechanism. In this case, $\beta\beta$-diphenylacrylonitrile (7) and 2,3,3-tricyano-1,1,4,4-tetraphenylbut-1-ene (8) were obtained in addition to the expected reduction product α-cyano-$\beta\beta$-diphenylpropionitrile (6) [equation (4)]. The formation of $\beta\beta$-diphenylacrylonitrile can be explained only by elimination of CN^- from the intermediate carbanion (6-A) [equation (5)]. The diphenyl-

acrylonitrile thus formed reacts in a fast acid–base type reaction with LDA to form the derived vinyl carbanion, which in turn adds as a nucleophile at C-α of the olefin

$$Ph_2C=C \begin{smallmatrix} CN \\ \\ CN \end{smallmatrix} \xrightarrow[0\ °C]{LDA-THF} Ph_2CH-CH(CN)_2 + $$
(5)   (6)

$$Ph_2C=CHCN + Ph_2C=C \begin{smallmatrix} CN \\ \\ C(CN)_2-CHPh_2 \end{smallmatrix} \quad (4)$$
(7)   (8)

(5) to yield (after protonation) the co-dimer (8). This co-dimer was obtained in a good yield by adding the olefin (5) to a solution of $Ph_2C=\bar{C}(CN)Li^+$ in THF at

The mechanism proposed [equation (3)] for the reduction of activated olefins by lithium amides is similar to that of the Meerwein–Pondorf–Verley reduction,[7] which was also applied to explain the reduction of non-enolizable ketones by lithium amides.[8]

EXPERIMENTAL

Ethyl α-cyano-ββ-diphenylacrylate (4),[9] α-cyano-ββ-diphenylacrylonitrile (5),[10] ethyl ββ-diphenylacrylate (2),[11] ββ-diphenylacrylonitrile (7),[12] and 2,2,6,6-tetramethylpiperidine [13] were prepared according to known methods. Lithium amides were prepared by addition of the amine to an equimolar solution of butyl-lithium. All experimental manipulation and the reaction apparatus were as previously described.[3]
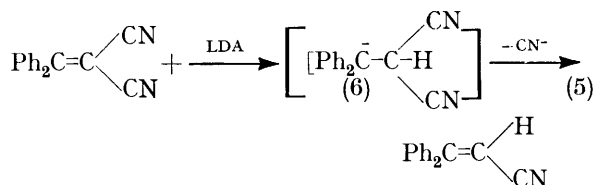
Reduction of Ethyl α-Cyano-ββ-diphenylacrylate (4).—A

Reduction of activated olefins by lithium amides

Olefin	10^3[olefin]/ mol l⁻¹	Lithium amide	10^3[Amide]/ mol l⁻¹	T/°C	t/min	Reduction products (%)
$Ph_2C=C \begin{smallmatrix} COOEt \\ CN \end{smallmatrix}$	2.00	LDA	6.00	−78	30	$Ph_2CH-CH(CN)COOEt$ (81)
		LDA ᵃ		−78		$Ph_2CH-CH(CN)COOEt$ (78)
		LTMP		−78		*b*
		LDA		0		$Ph_2CH-CH(CN)COOEt$ (85)
		LBCA		−78		$Ph_2CH-CH(CN)COOEt$ (80)
$Ph_2C=C \begin{smallmatrix} COOEt \\ C-Ph \\ O \end{smallmatrix}$	0.87	LDA	2.60	−78		$Ph_2CH-CH(COPh)COOEt$ (77)
		LTMP		−78		*b*
$Ph_2C=C(CN)_2$	0.50	LDA	1.00	0	45	$Ph_2CH-CH(CN)_2$ ᶜ (43)
$Ph_2C=C \begin{smallmatrix} H \\ COOEt \end{smallmatrix}$		LDA		−78		*b*
$Ph_2C=C \begin{smallmatrix} H \\ CN \end{smallmatrix}$				−78		*b*

ᵃ Diethyl ether was used as solvent. ᵇ No reduction. ᶜ Other products isolated were $Ph_2C=CH-CN$ (18%) and $Ph_2C=C(CN)C-(CN)_2-CH(Ph)_2$ (36%).

−78 °C. Various reactions of this vinyl carbanion as a nucleophile were recently described.[3]

ββ-Diphenylacrylonitrile (7) and ethyl ββ-diphenylacrylate (2) were not reduced by LDA, presumably because the corresponding non-electrophilic derived vinyl carbanions were formed in a relatively fast acid–base

$$Ph_2C=C \begin{smallmatrix} CN \\ CN \end{smallmatrix} + \xrightarrow{LDA} \left[Ph_2\bar{C}-C \begin{smallmatrix} CN \\ H \\ CN \end{smallmatrix} \right] \xrightarrow{-CN^-}$$
(6)   (5)

$$Ph_2C=C \begin{smallmatrix} H \\ CN \end{smallmatrix}$$

reaction prior to the hydride-transfer reaction. It was however suggested that ββ-diphenylacrylonitrile could react with a hydride ion to yield its reduced derivative, ββ-diphenylpropionitrile.[4]

solution of (4) (0.550 g, 2×10^{-3} mol) in THF (10 ml) was added dropwise during 3 min to a solution of LDA (6 × 10^{-3} mol) in THF (30 ml) at −78 °C. After stirring for 30 min at −78 °C, the reaction mixture was acidified followed by extraction with ether. The crude residue recovered from the ethereal extracts was crystallized from light petroleum–carbon tetrachloride to give ethyl α-cyano-ββ-diphenylpropionate (9) (0.45 g, 81%), m.p. 75—77 °C (lit.,[14] 75—77 °C), τ(CDCl₃) 8.95 (3 H, t, *J* 8 Hz), 5.94 (2 H, q, *J* 8 Hz), 5.80 (1 H, d, *J* 8.5 Hz), 5.30 (1 H, d, *J* 8.5 Hz), and 3.10 (10 H, m).

Reaction of Ethyl ββ-Diphenylacrylate (2) with Methyl Benzoate in the Presence of Lithium Amides.—A solution of (2) (0.502 g, 2×10^{-3} mol) in THF (10 ml) was added dropwise during 3 min into a solution of LDA (6 × 10^{-3} mol) in THF (30 ml) at −78 °C. The mixture was stirred for 15 min, methyl benzoate (0.732 g, 6 × 10^{-3} mol) was added, and stirring was continued for another 30 min. The reaction mixture was acidified and extracted with ether.

The crude residue recovered from the ethereal extracts was washed several times with light petroleum to remove unchanged methyl benzoate. The residue left behind was separated by chromatography on a silica column, to give ethyl α-benzoyl-ββ-diphenylpropionate (3) (0.150 g, 21%), m.p. 133—134 °C (from ethanol) (lit.,[15] 135—136 °C), identical with an authentic compound,[15] τ(CDCl₃) 9.05 (3 H, t, J 7.5 Hz), 6.05 (2 H, q, J 7.5 Hz), 4.85 (1 H, d, J 12 Hz), 4.50 (1 H, d, J 12 Hz), 2.80—2.20 (13 H, m), and 1.90—1.60 (2 H, m).

Lithium tetramethylpiperidide (LTMP) (prepared by addition of an equivalent amount of butyl-lithium into a solution of tetramethylpiperidine in THF) was used as base, instead of LDA. The same concentrations of reactants and experimental conditions were used as described above. The crude product recovered from the ethereal extracts was purified by column chromatography to yield ethyl α-phenyloxy-ββ-diphenylacrylate (1) (0.310 g, 43%), m.p. 108—109 °C (from CCl₄), τ(CDCl₃) 9.05 (3 H, t, J 7.5 Hz), 6.00 (2 H, q, J 7.5 Hz), 3.00—2.50 (m, 13 H), and 2.00—2.30 (m, 2 H).

Reduction of Ethyl α-Benzoyl-ββ-diphenylacrylate (1).—A solution of the olefin (1) (0.310 g, 0.87 × 10⁻³ mol) in THF (5 ml) was added dropwise during 3 min to a solution of LDA (2.6 × 10⁻³ mol) in THF (25 ml) at −78 °C. The mixture, which became dark, was stirred for 50 min, acidified with dilute hydrochloric acid, and extracted with ether. The residue recovered from the ethereal extracts was separated by chromatography on a silica column to give ethyl α-benzoyl-ββ-diphenylpropionate (3) (0.25 g, 77%), m.p. 133—134 °C (from ethanol) (lit.,[15] 135—136 °C), identical with the authentic compound.[15]

Reduction of α-Cyano-ββ-diphenylacrylonitrile (5).—The olefin (5) (1.15 g, 0.50 × 10⁻³ mol) in THF (10 ml) was added dropwise during 3 min to a solution of LDA (1 × 10⁻³ mol) in THF (30 ml) at 0 °C. The mixture which became dark, was stirred for 45 min at 0 °C, acidified, and extracted with ether. The residue recovered from the ethereal extracts was separated by chromatography on a silica column using light petroleum–methylene chloride as eluant. The overall conversion of (5) was 97%. The products isolated were ββ-diphenylacrylonitrile (7) (0.19 g, 18%); α-cyano-ββ-diphenylpropionitrile (6) (0.51 g, 43%), m.p. 79—80 °C (from ethanol) (lit.,[16] 81—82 °C), τ(CDCl₃)

5.60 (1 H, d, J 7.5 Hz), 5.40 (1 H, d, J 7.5 Hz), and 2.70—2.40 (10 H, m), 2,3,3-tricyano-1,1,4,4-tetraphenylbut-1-ene (8) (0.41 g, 36%), m.p. 225—227 °C (decomp.) (from chloroform–petroleum), τ(CDCl₃) 5.90 (1 H, s), 3.50—3.20 (2 H, m), and 2.90—2.50 (18 H, m).

2,3,3-*Tricyano-1,1,4,4-tetraphenylbut-1-ene* (8).—A solution of ββ-diphenylacrylonitrile (0.41 g, 2 × 10⁻³ mol) in THF (10 ml) was added dropwise during 2 min to a solution of LDA (4 × 10⁻³ mol) in THF (25 ml) at −78 °C. The dark mixture was stirred for 5 min and a solution of α-cyano-ββ-diphenylacrylonitrile (5) (0.46 g, 2 × 10⁻³ mol) in THF (10 ml) was added dropwise during 2 min. The mixture was stirred for 15 min, acidified with dilute hydrochloric acid, and extracted with ether. The crude product recovered from the ethereal extracts was crystallized to yield 2,3,3-tricyano-1,1,4,4-tetraphenylbut-1-ene (8) (0.78 g, 90%), m.p. 225—227 °C (decomp.) (from chloroform–light petroleum). Its spectral data were identical to the sample prepared above.

REFERENCES

[1] R. R. Schmidt and J. Talbiersky, *Angew. Chem. Internat. Edn.*, 1977, **16**, 853.
[2] R. R. Schmidt and J. Talbiersky, *Angew. Chem. Internat. Edn.*, 1978, **17**, 204.
[3] U. Melamed and B. A. Feit, *J.C.S. Perkin I*, 1978, 1232.
[4] U. Melamed and B. A. Feit, *J.C.S. Perkin I*, 1978, 1228.
[5] J. Smid, in ' Ions and Ion Pairs in Organic Reactions,' ed. M. Swarc, Wiley, 1972, p. 100.
[6] E. F. Silversmith and D. Smith, *J. Org. Chem.*, 1958, **23**, 427.
[7] A. L. Wilds, *Org. Reactions*, 1944, **2**, 178.
[8] E. P. Woo and K. T. Mak, *Tetrahedron Letters*, 1974, 4095.
[9] E. J. Crage, C. M. Robb, and J. M. Spargue, *J. Org. Chem.*, 1950, **15**, 381.
[10] P. Michaelis, K. Pape, and F. Pleuger, *Annalen*, 1928, **462**, 267.
[11] E. Bergmann, H. Hoffmann, and H. Meyer, *J. prakt. Chem.*, 1932, **135**, 245.
[12] C. Runti and L. Sindellari, *Bull. Chem. Pharm.*, 1960, **99**, 499.
[13] H. K. Hall, *J. Amer. Chem. Soc.*, 1957, **79**, 5444.
[14] E. P. Kohler and M. Reimer, *Amer. Chem. J.*, 1905, **33**, 333.
[15] E. P. Kohler and M. Tishler, *J. Amer. Chem. Soc.*, 1932, **54**, 1594.
[16] E. Campaigne and W. L. Roelofs, *J. Org. Chem.*, 1965, **30**, 396.