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ZINC-INDUCED ADDITIONS OF α-HALOGENOKETONES TO CONJUGATED ENYNES AND DIENES

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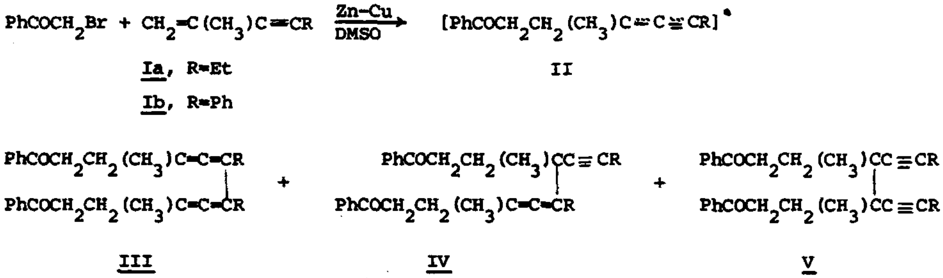
We reported recently[1] that, in contrast to the well known ionic reactivity of metal enolates, the reaction of aromatic α-halogenoketones with Zn-Cu couple in DMSO solution results in homolytic cleavage leading to α-ketomethylene free-radicals.

We should now like to report on the specific manner by which such species, formed from phenacyl bromide and Zn-Cu couple, react with conjugated enynes and dienes. The investigation of these reactions was considered of interest because the intermediate formation of resonance-stabilized adduct radicals may compete successfully with the formerly observed[1] dimerization of phenacyl-radicals; moreover, only few addition reactions of enynes of proven radical nature are known.[2]

When an excess of phenacyl bromide (5 equiv.) was added under inert atmosphere to a mixture of enyne <u>I</u> (1 equiv.) and Zn-Cu couple[3] (30 equiv.) in DMSO (3 ml for each equiv. of <u>I</u>)- the products <u>III</u>-<u>V</u> were formed. The total yields were 78% (for <u>IIIa</u>-<u>Va</u>) and 91% (for <u>IIIb</u>-<u>Vb</u>). No other adducts or telomers were detected. The structure of the products shows that the addition step occurs at the olefin teminus leading to propargylic radicals (II), which, in absence of an appropriate reagent (e.g., scavenger, hydrogen donor or oxidizing agent), dimerize either at the allenic or propargylic terminus. Although the relative yields of all isomers were not determined, the ratio of acetylene:allene moieties in the product mixture was found to be about 60:40 in both <u>a</u> and <u>b</u> series (n.m.r. evidence) and pure isomers could be separated on a silica G column. Mass spectra, n.m.r. and u.v. data were in accord with



$$PhCOCH_2Br + CH_2{=}C(CH_3)C{\equiv}CR \xrightarrow[DMSO]{Zn-Cu} [PhCOCH_2CH_2(CH_3)C{\doteq}C{\doteq}CR]^{\bullet}$$

<u>Ia</u>, R=Et

<u>Ib</u>, R=Ph

II

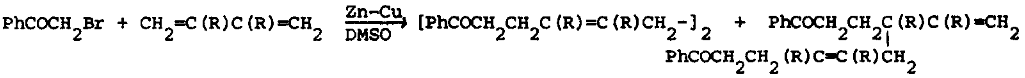
$$\begin{matrix} PhCOCH_2CH_2(CH_3)C{=}C{=}CR \\ | \\ PhCOCH_2CH_2(CH_3)C{=}C{=}CR \end{matrix} + \begin{matrix} PhCOCH_2CH_2(CH_3)CC{\equiv}CR \\ | \\ PhCOCH_2CH_2(CH_3)C{=}C{=}CR \end{matrix} + \begin{matrix} PhCOCH_2CH_2(CH_3)CC{\equiv}CR \\ | \\ PhCOCH_2CH_2(CH_3)CC{\equiv}CR \end{matrix}$$

<u>III</u> <u>IV</u> <u>V</u>

the assigned structures. The diallene IIIa, mp 130° (meso or racemic), had a u.v. absorption peak at 227 nm (ε=27000,EtOH), in addition to the peak at 242 nm (ε=26500; PhCO), shown also by IVa and Va. In the p.m.r. spectrum of IIIa ($CDCl_3$) the tertiary methyl protons appear at δ 1.70 (s) while in the diastereomeric diacetylenes Va (mp 124° and 112°) the corresponding signals are at δ 1.30 and δ 1.27 respectively and at δ 1.70 and 1.27 in IVa (isomeric mixture). In compounds IIIb-Vb the tertiary methyl protons appear at δ 1.50 and 1.53 (in acetylenic moieties) and δ 1.88 (in allenic moieties).

The allene and acetylene bands were inactive in i.r.[5] and therefore the structural assignments were confirmed by ^{13}C n.m.r., by help of the characteristic chemical shifts of allenic and acetylenic carbons.[6] In IIIa the signals at 199.2, 102.0 and 106.4 ppm were assigned to allenic carbons while in Va the acetylenic carbons absorb at 81.8 and 84.7 ppm (relative to TMS, in $CDCl_3$). In IVa, after reducing (LAH) the interfering carbonyl groups, the central allenic carbon absorbed at 194 ppm. Diallene IIIa is stable on heating (150°) and is not sensitive in air. To this date, few methods for the formation of conjugated diallenes are available.[7]

The reaction of phenacyl bromide with conjugated dienes takes place in similar conditions[8] but the dimerization occurs overwhelmingly at the methylene terminus of the allylic radical adduct:



$$PhCOCH_2Br + CH_2{=}C(R)C(R){=}CH_2 \xrightarrow[DMSO]{Zn-Cu} [PhCOCH_2CH_2C(R){=}C(R)CH_2-]_2 + \begin{array}{l} PhCOCH_2CH_2C(R)C(R){=}CH_2 \\ PhCOCH_2CH_2(R)C{=}C(R)CH_2 \end{array}$$

VIa, R=Ph	VIIa (73% y.)	VIIIa (not detected)
VIb, R=Me	VIIb (55% y.)	VIIIb (7% y.)

All configurational isomers (see Table) were separated on a column of neutral alumina containing 10% $AgNO_3$. The assignments for VIIa isomers followed from the relative shielding in the n.m.r. of the ethylene groups (br.s.) when located cis to phenyl groups. Unequal deshielding by a shift reagent in n.m.r. was used for configurational assignments of VIIb isomers: on addition of $Eu(fod)_3$, the central ethylene group in the isomeric mixture (δ 2.04, s, br) separated into three distinct singlets, each corresponding to the central ethylene group of a specific isomer, as found from the n.m.r. spectra of the pure isomers, taken in identical conditions. These shifts are rationalized by the ability of $Eu(fod)_3$ to form chelates with two electron-donating groups.[9] The preferred coiled conformation of the cis-cis isomer VIIb (see Fig.) probably enhances this chelating ability, while the elongated conformation of the trans-trans isomer inhibits it. The decrease of the chelating ability in the order cis-cis > cis-trans > trans-trans isomer should affect in the same manner the deshielding of the central ethylene group.

Table

Isomer	VIIa		VIIb*	
	Rel. yield (%)	m.p.	Rel. yield (%)	m.p.
cis-cis	28	152°	15	91°
cis-trans	60	126°	47	b.p. 172°/1 mm
trans-trans	12	232°	27	114°

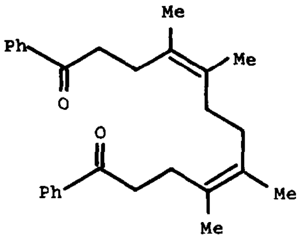


Fig. cis-cis VIIb

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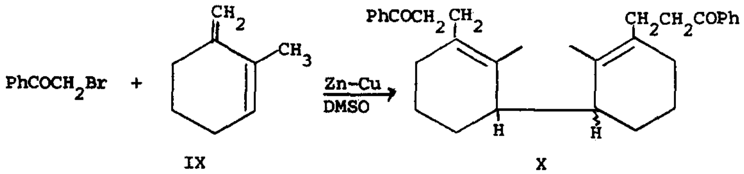
* Compound VIIIb m.p. 85°, accounts for 11% rel. yield.

It is assumed that the regiospecific coupling of allylic radicals is promoted by factors of stereosensitivity and product stability, while additional factors[10] are responsible for the observed distribution of addition at the two termini of the propargylic radical. The formation of all isomers and the predominance of cis-trans isomers suggests that rotational equilibrium is achieved before dimerization occurs.

The importance of the steric factor in the coupling step was also emphasized in the addition of the $PhCOCH_2$ radical to IX, which occurs at the exocylic methylene and is followed by coupling at the less substituted terminus of the adduct radical leading to a separable mixture[11] of (±) and meso X (62% y.), m/e 454 (M^+), 227 (base peak), δ 1.62 (s, CH_3).



Radicals generated by help of the Fenton reagent[12] or via organic hydroperoxides[13] react with dienes by a similar pathway. Our results thus provide a further confirmation on the unprecedented zinc-induced free-radical formation from α-halogenoketones.

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References and Footnotes

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