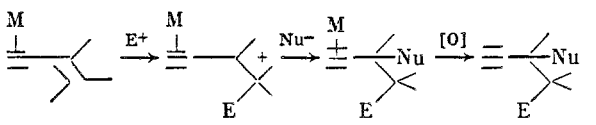
SHORT PATH TO THE SYNTHESIS OF BI- AND TRICYCLIC COMPOUNDS CONTAINING THE 3-OXABICYCLO[3.3.0]OCTENE FRAGMENT FROM CONJUGATED ENYNES BY SUCCESSIVE Ad_E REACTION AND [2+2+1]-CYCLOADDITION

W. A. Smit, S. O. Simonyan, G. S. Mikaelyan,
S. S. Mamyan, A. S. Gybin, A. S. Shashkov,
and R. Caple

UDC 542.91:547.518

Earlier [1, 2] a general method was developed for the production of various polyfunctional acetylenes (PFA) by the Ad_E reaction of hexacarbonyldicobalt (HCDC) complexes of conjugated enynes, conducted as a sequence of independenct stages of addition of the electrophile E^+ and nucleophile Nu^- with the intermediate formation of cationoid intermediates (CI).

Scheme 1



$E^+ = RCO^+, R^+, NO_2^+, ArS^+$, $Nu^- = OH^-, OR^-, \bar{C}H_2COR$; $M = CO_2(CO)_6$.

The prospects for the preparative use of such polyfunctional acetylenes, determined by the presence of such reactive functions as the triple bond, carbonyl group, and propargyl group, are obvious. However, as seen from scheme 1, the products produced directly as a result of the Ad_E reaction are the hexacarbonyldicobalt complexes of the polyfunctional acetylene. It therefore seemed expedient to study first the possibilities of synthetic use of these compounds, determined by the presence of the transition metal.

Among the reactions characteristic of the HCDC complexes of alkynes [3], the [2+2+1]-cycloaddition to alkenes (the Khand—Pauson reaction) is of special interest for synthesis. This reaction makes it possible to obtain various derivatives of cyclopentenones (the intermolecular version [4]) or bicyclo[3.3.0]octenones (the intramolecular version [5]) from simple precursors.

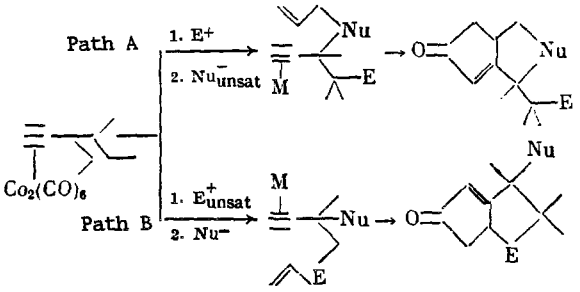
Scheme 2

It is easy to see that the general method for the production of the HCDC complexes of polyfunctional acetylenes can be used in principle for the production of a wide range of substrates for the intramolecular Khand—Pauson reaction, if nucleophiles and/or electrophiles containing a double bond (Nu^-_{unsat} or E^+_{unsat} respectively) are used as addends (scheme 3).

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 334-344, February, 1989. Original article submitted September 1, 1987.

0568-5230/89/3802-0285$12.50

Scheme 3

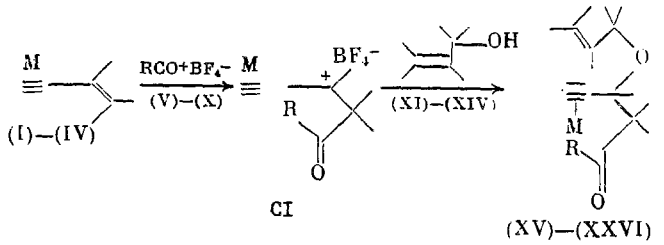


It is known that the intramolecular version of the Khand—Pauson reaction takes place particularly readily for the HCDC complexes of allyl propargyl ethers [6, 7]. The task of the present work was therefore to determine the possibility of using path A for the production of adducts containing the allyl propargyl ether fragment (Nu^-_{unsat} = $OC-\overset{|}{\underset{|}{C}}=C\diagup$), and also the suitability of the previously developed method for the realization of [2+2+1]-cycloaddition on the surface of adsorbents [7-9] for such polyfunctional derivatives.

As initial substrates we used the HCDC complexes of vinyl-, isopropenyl-, cyclopentenyl-, and cyclohexenylacetylene [(I, II, III, IV) respectively] and studied their Ad_E reactions with acylium salts [acetyl (V), propionyl (VI), isobutyryl (VII), isovaleryl (VIII), acryloyl (IX), and crotonoyl (X) tetrafluoroborates]* as electrophiles and allyl (XI), methallyl (XII), and crotyl (XIII) alcohols and also dimethylvinylcarbinol (XIV) as nucleophiles.

The reactions of (I-IV) with the acylium salts (V-X) were conducted under the previously described [1, 2] conditions (methylene chloride, —70°C). It was found that the cationoid intermediate formed during the addition of the acyl cation at the double bond of the HCDC complexes of the enynes are capable of reacting with O-nucleophiles of type (XI-XIV)** with the production of the adducts (XV-XXVI), the structures of which correspond to 1,2-addition of the aryl cation E^+ and the allyloxy anion $^-Nu_{unsat}$ according to the general scheme 4.

Scheme 4



M = $Co_2(CO)_6$.

The developed method of acylallyloxylation permits wide variations in the nature of all three reaction components and makes it possible to obtain structurally different HCDC complexes of allyl propargyl ethers, containing an α-acylalkyl residue at the propargyl center, according to the same type of scheme (Table 1).

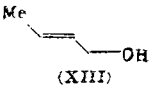
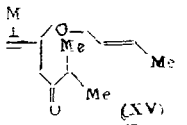
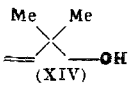
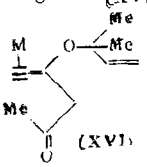
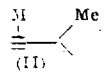
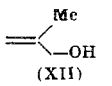
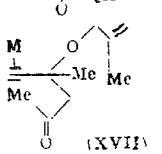
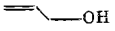
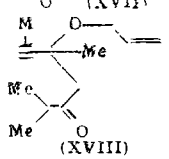
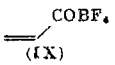
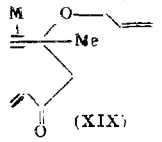
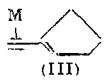
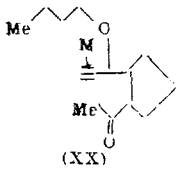
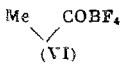
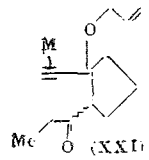
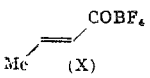
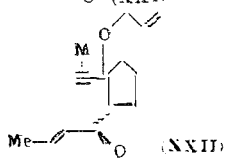
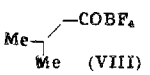
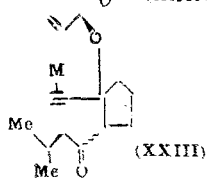
The adducts (XV-XXVI) proved labile, and this did not make it possible to characterize them by analytical or spectral methods. However, their structures were proved unambiguously by means of the data from the mass spectra and the PMR spectra of the corresponding β-ethynyl-β-allyloxy ketones obtained from (XV-XXVI) by oxidative decomplexation with cerium(IV) ammonium nitrate [2] (yield 80-90%).† The monocyclic derivatives (XX-XXVI) are mixtures of stereoisomers correspondign to syn- and anti-addition of the addends at the double bond of the initial enyne. By analogy with published data [10] the structure of the anti-adduct was adopted for the main isomer.

*The choice of reagents of the $RCO^+BF_4^-$ type was due to the fact that according to [1, 2] the widest variations in the nature of the introduced electrophilic residue RCO^+ are possible in this case.

**The "quenching" of the cationoid intermediates takes place readily with the addition of dry potassium carbonate to the reaction mixture to combine with the released HBF_4.

†In all cases the mass spectra contained the molecular ion peaks.

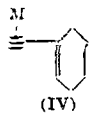
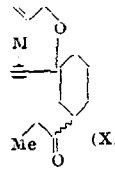
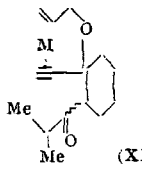
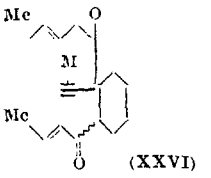
TABLE 1

Initial substances: complex of enyne*	Initial substances: acylium salt	Allyl alcohol	Product	Yield, %**
 (I)	$Me_2CHCOBF_4$ (VII)	 (XIII)	 (XV)	92
(I)	$MeCOBF_4$ (V)	 (XIV)	 (XVI)	69
 (II)	(V)	 (XII)	 (XVII)	72
(II)	(VII)	 (XI)	 (XVIII)	59
(II)	 (IX)	(XI)	 (XIX)	50
 (III)	(V)	(XIII)	 (XX)	77
(III)	 (VI)	(XI)	 (XXI)	33
(III)	 (X)	(XI)	 (XXII)	54
(III)	 (VIII)	(XI)	 (XXIII)	55

Attempts to realize the intramolecular [2+2+1]-cycloaddition for the adducts (XV-XIX) under the traditional conditions for this reaction in solution (octane, 60-100°C, 6-8 h) [4, 6] proved unsuccessful on account, evidently, of the ease of elimination of alcohol from the β-allyloxy ketone fragment in the structure. Conversely, under our previously developed conditions for the Khand—Pauson reaction on the surface of chromatographic adsorbents [7-9] the cyclization of (XV-XIX) took place smoothly and led to the formation of the expected products, i.e., the substituted 3-oxabicyclo[3.3.0]oct-5-en-7-ones (XXVII-XXXI) with satisfactory yields.[†]

[†]All the yields are given on the isolated products; the reaction conditions were not optimized.

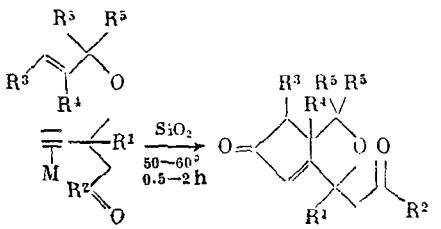
Continued Table 1

Initial substance: complex of enyne*	Initial substance: acylium salt	Allyl alcohol	Product	Yield, %**
 (IV)	(VI)	(XI)	 (XXIV)	64
(IV)	(VIII)	(XI)	 (XXV)	71
(IV)	(X)	(XIII)	 (XXVI)	40

*M = $Co_2(CO)_6$

**The yields are given on the isolated chromatographically pure adduct. The conditions for the production of (XV-XXVI) were not optimized.

Scheme 5

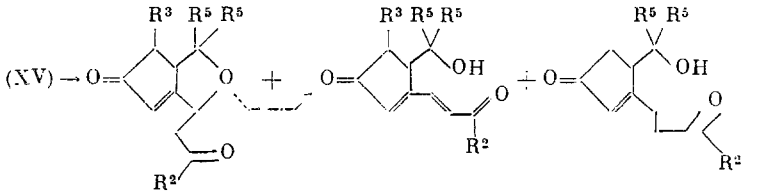


(XV)—(XIX) (XXVII)—(XXXI)

$R^1 = R^4 = R^5 = H$, $R^2 = Me_2CH$, $R^3 = Me$ (XV), (XXVII), 47%; $R^1 = R^3 = R^4 = H$, $R^2 = R^5 = Me$ (XVI), (XXVIII), 55%; $R^1 = R^2 = R^4 = Me$, $R^3 = R^5 = H$ (XVII), (XXIX), 61%; $R^1 = Me$, $R^2 = Me_2CH$, $R^3 = R^4 = R^5 = H$ (XVIII), (XXX), 39%; $R^1 = Me$, $R^2 = CH_2 = CH$, $R^3 = R^4 = R^5 = H$ (XIX), (XXXI), 43%; $M = Co_2(CO)_6$.

During the cyclization of the isopropenylacetylene derivatives (XVII-XIX) it was not possible to detect the formation of cyclic side products, and the major complication in the reaction, i.e., the partial elimination of the β-allyloxy group in the acyclic precursors, is evidently the reason for the relatively low yields of the adducts (39-61%). The vinylacetylene derivatives (XV) and (XVI) are clearly more stable, and almost complete transformation according to the [2+2+1]-cycloaddition scheme is observed in these cases. Here, however, apart from the desired bicyclic products (XXVII) [or (XXVIII)] the monocyclic dienones (XXXII) [or (XXXIII)], i.e., the products from intramolecular fragmentation of (XXVII) [or (XXVIII)] (Scheme 6), are also formed. In addition, partial [2+2+1]-cycloaddition, accompanied by hydrogenolysis of the ether bond [cf. the cyclization of allyl propargyl ethers [11], leading to the monocyclic products (XXXIV) [or (XXXV)] is also observed.

Scheme 6



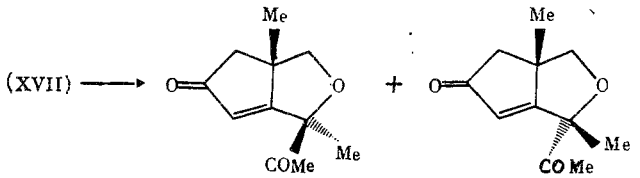
(XXVII), 47%
(XVI) → (XXVIII), 53%

(XXXII), 26%
(XXXIII), 18%

(XXXIV), 26%
(XXXV), 21%

The bicylic products (XXVII-XXXI) are mixtures of two stereoisomers (with respect to C^4) in ratios of 1.5-2.2:1 (PMR). For (XXIX) it was possible to separate this mixture (TLC) and to demonstrate the configuration of the isomers by means of the results from the nuclear Overhauser effect (Scheme 7).

Scheme 7

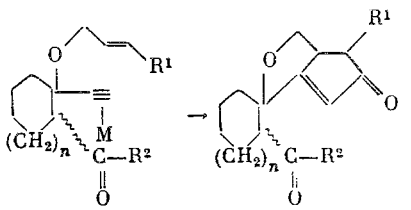


(XXIXa) (19%) (XXIXb) (42%)

It was assumed that the cyclization of the adducts (XVIII) and (XIX) goes in a similar direction, i.e., the isomers (XXXb) and (XXXIb) with the cis arrangement of the methyl groups at C^1 and C^4 are formed preferentially. The stereochemistry of the adducts (XXVII) and (XXVIII) was not established.

The derivatives of cyclopentenyl- and cyclohexenylacetylene (XX-XXVI) (Table 1) enter into the Khand—Pauson reaction, giving the spirocoupled tricyclic products (XXXVI-XLII) (Scheme 8). For the cyclization of these substrates it is possible to use also the standard procedure for thermolysis in hexane solution, but here it is necessary to conduct the reaction under more rigorous conditions (60°C, 8 h) than on the surface of silica (50°C, 2 h).

Scheme 8



(XX)—(XXVI) (XXXVI)—(XLII)

$n = 0$, $R^1 = R^2 = Me$ (XX), (XXXVI), 68%*; $n = 0$, $R^1 = H$, $R^2 = Et$ (XXI), (XXXVII), 29%; $n = 0$, $R^1 = H$, $R^2 = MeCH{=}CH$ (XXII), (XXXVIII), 44%*; $n = 0$, $R^1 = H$, $R^2 = Me_2CHCH_2$ (XXIII), (XXXIX), 45%; $n = 1$, $R^1 = H$, $R^2 = Et$ (XXIV), (XL), 31%; $n = 1$, $R^1 = H$, $R^2 = Me_2CHCH_2$ (XXV), (XLI), 43%; $n = 1$, $R^1 = Me$, $R^2 = MeCH{=}CH$ (XXVI), (XLII), 48%*.

Analysis of the PMR spectra of compounds (XXXV-XLII) showed that a mixture of two stereoisomers of the products is formed in all cases. The ratio of the isomers (3:1) corresponds to the ratio of the stereoisomers in the initial substrates (see above).

In order to determine the characteristics of the stereochemistry of the transformations shown in Scheme 8 the adduct (XXIII) was separated into the individual stereoisomers (XXIIIa) and (XXIIIb) (3:1) by TLC. The cyclization of both stereoisomers (hexane, 60°C) led to the formation of the individual (PMR) isomers (XXXIXa) (yield 22%) and

*In these cases the cyclization was conducted on silica.

(XXXIXb) (yield 43%). On the basis of data on the preference for the formation of the anti-adducts during the production of (XXIII) the structure with the trans orientation of the acyl residue and the ether oxygen was adopted for the tricyclic adduct (XXXIXa). The individual isomer (XLIa) presumably with the same stereochemistry was obtained during the cyclization of the main isomer (XXVa).

Thus, a method was developed which makes it possible to add various acyl and allyloxy addends at the double bond of the HCDC complexes of conjugated enynes, and the possibility of converting the obtained adducts by an intramolecular Khand—Pauson reaction into bi- and tricyclic compounds containing the 3-oxabicyclo[3.3.0]octane fragment was demonstrated. A new approach was thereby created for the synthesis of fairly complex compounds from available precursors (the HCDC complexes of conjugated enynes, acylium tetrafluoroborates, and allyl alcohols) on the basis of a general scheme (path A, Scheme 3) which includes only two stages and makes it possible to vary the structure of the units used in the synthesis within wide limits.

The possibilities for the use of the alternative approach (path B, Scheme 3) will be discussed in the next communication.

EXPERIMENTAL

The ^1H and ^{13}C spectra were recorded on a Bruker WM-250 spectrometer. The chemical shifts (δ) are given with reference to TMS for solutions in deuterochloroform, and the spin-spin coupling constants are given in hertz. The mass spectra were recorded on a Varian MAT-CH6 instrument. Analytical TLC was conducted on Silufol plates (preparative, unfixed layer of sorbent, SiO_2; LSL 40/100 for Silpearl). The elemental analyses were conducted on an automatic Perkin—Elmer model 240 automatic analyzer.

The HCDC complexes (I-IV) were obtained by the previously described method (e.g., see [2]). The acylallyloxylation of the HCDC complexes of the conjugated enynes was realized by typical procedures, examples of which are given below.

HCDC Complex of 3-Methyl-3-methallyloxyhex-1-yn-5-one (XVII). To a solution of acetyl fluoride (0.12 g, 2 mmoles) in methylene chloride (15 ml), stirred at —70°C, we added a solution of the complex (II) (0.5 g, 1.42 mmoles) in methylene chloride (10 ml). We then introduced gaseous boron trifluoride (200 ml, 8 mmoles) into the mixture by means of a syringe. After 15 min we added to the mixture a solution of methallyl alcohol (XII) (0.5 g, 7 mmoles) in methylene chloride (10 ml) and 0.2 g of dry potassium carbonate. Thin-layer chromatography showed that almost all the cationoid intermediate had reacted with (XII) after 20 min. The mixture was then treated with a saturated aqueous solution of sodium bicarbonate and extracted with ether. The extract was dried over magnesium sulfate, and after removal of the solvent the residue (a dark-red oil) was separated by TLC (1:1 benzene—hexane). We obtained 0.5 g (72%) of the adduct (XVII) (R_f = 0.62, 3:1 hexane—ether).

HCDC Complex of 3-(3,3-Dimethylallyloxy)hex-1-yn-5-one (XVI). To a stirred solution of the complex (I) (1 g, 2.96 mmoles) in methylene chloride (10 ml) at —78°C we added a solution of acetyl fluoride (0.31 g, 5 mmoles) in methylene chloride (10 ml), and we then introduced boron trifluoride (200 ml, 8 mmoles) into the mixture. After 45 min we added to the mixture a solution of the carbinol (XV) (0.86 g, 10 mmoles) in methylene chloride (30 ml) and 0.5 g of dry potassium carbonate. After 40 min the mixture was treated with a saturated solution of sodium bicarbonate and extracted with ether, and the extract was passed through a layer of silica gel (40/100). After removal of the solvents the remaining dark-red oil was separated by TLC (4:1 hexane—ether). We obtained 0.95 g (69%) of the adduct (XVI) (R_f = 0.67, 3:1 hexane—ether).

HCDC Complex of 1-Ethynyl-1-allyloxy-2-isovalerylcyclopentane (XXIII). To a stirred solution of isovaleryl fluoride (0.34 g, 3.2 mmoles) in a CH_2Cl_2—CH_3NO_2) mixture (2:1, 15 ml) at —70°C we added a solution of the complex (III) (0.8 g, 2.1 mmoles) in methylene chloride (15 ml), and we then introduced boron trifluoride (200 ml, 8 mmoles) into the mixture by means of a syringe. After 20 min we added to the mixture a solution of the alcohol (VIII) (2.9 g, 50 mmoles) in methylene chloride (5 ml) cooled to —70°C. Thin-layer chromatography (with treatment of the sample of the reaction mixture with water) showed a very small content of the desired adduct in the reaction mass, and the temperature was therefore raised to —40°C and was again lowered to —70°C after 10 min. After 20 min the mixture was treated with a saturated aqueous solution of sodium bicarbonate and extracted with ether, and the extract was dried over magnesium sulfate. After removal of the solvents the remaining dark-red oil was separated by TLC (1:1 benzene—petroleum ether). We obtained 0.45 g (41%) of the main isomer (XXIIIa) (R_f = 0.64, 1:1 benzene—petroleum ether) and 0.13 g (14%) of the isomer (XXXIIIb) (R_f = 0.61, 1:1 benzene—petroleum ether).

The obtained HCDC complexes (XV-XXVI) (Table 1) could not be characterized by means of the PMR spectra on account of the considerable broadening of the signals. Their identities were established by means of the mass spectra [all the spectra contained a strong peak with m/e M^+ —168 (6CO)], and also by means of the result from subsequent

TABLE 2. ^{1}H NMR Spectra (δ, ppm, J, Hz) of the Derivatives of 3-Oxabicyclo[3.3.0]octane*

Compound	H^1	H^2	H^4	H^6	H^8	Substitute. $-CH_2COR$ at C	
(XXVII)	3,0 m	4,3 dd 3,35 dd AB part of ABX system J_{AB} = 16, $J_{AX} = J_{BX} = 8$)	5,05 t (J = 7)	6,1 t (J = 2)	2,2 m	1,27 d (J = 7)	2,8 d 2,6m, 1,1 d 1,15 d (R=CHMe$_2$)
(XXVIII)	3,05 m	—	4,92 t (J = 7)	5,98 dd (J = 1,25; 2,5)	2,0—3,0 m	0,9 s 1,35 s	2,0—3,0 m 2,1 s (R=Me)
(XXIXa)	—	3,5 d 3,9 d (AB, J = 9)	—	6,05 s	2,4 dd (AB, J = 16)	1,37 s 1,45 s	3,05 d 2,9 d 2,2 s (AB, J = 16) (R=Me)
(XXIXb)	—	3,63 d 3,95 d (AB, J = 8)	—	5,88 s	2,39 d 2,4 d (AB, J = 17)	1,41 s, (at C^1), 1,6 s (at C^4)	2,75 d 2,81 d 2,18 s (AB, J = 16) (R=Me)
(XXX)	3,45 m	4,2 m 3,5 m	—	5,92 d (J = 2)	2,2 dd 2,6 dd	1,5	2,95 dd, 2,6m, 1,1 d 1,15 d (AB, J = 16) (R=CHMe$_2$)
(XXXI)	3,4	4,2 m 3,4 m	—	5,95 d (J = 2)	2,2 dd and 2,6 dd	1,5	3,0 m 6,35 dd, 6,2 d 6,05 d (R=CH=CH$_2$)

*The signals of the predominant isomer are given for (XXVII), (XXVIII), (XXX) and (XXXI); the assignment of the signals was made on the basis of the data from {^{1}H—^{1}H} double resonance and NOE for the individual (XXIXa) and (XXIXb).

TABLE 3. Elemental Analyses and Characteristics of the Mass Spectra of the Obtained Products

Compound	Found/Calculated, %		Molecular formula	M+
	C	H		
(XXVII)	69,97/70,24	8,42/8,16	$C_{13}H_{18}O_3$	232
(XXVIII)	67,48/68,02	7,61/7,26	$C_{11}H_{14}O_3$	194
(XXIX)	68,46/69,20	7,95/7,74	$C_{12}H_{16}O_3$	208
(XXX)	70,49/70,24	8,03/8,16	$C_{15}H_{18}O_2$	232
(XXXI)	—	—	$C_{12}H_{14}O_3$	206
(XXXIIa)	65,21/64,23	6,94/7,18	$C_{15}H_{20}O_4$	264
(XXXIIIa)	65,90/66,44	8,36/8,18	$C_{13}H_{18}O_4$	246
(XXXIVa)	67,77/67,64	7,96/8,32	$C_{15}H_{22}O_4$	266
(XXXVa)	63,84/64,64	7,63/7,26	$C_{13}H_{16}O_4$	248
(XXXVI)	71,63/71,77	8,15/7,74	$C_{14}H_{18}O_3$	234
(XXXVII)	71,57/71,77	8,00/7,74	$C_{14}H_{18}O_3$	234
(XXXVIII)	—	—	$C_{15}H_{18}O_3$	246
(XXXIX)	73,07/73,25	8,44/8,45	$C_{16}H_{22}O_3$	262
(XL)	—	—	$C_{15}H_{20}O_3$	248
(XLI)	73,67/73,88	9,00/8,75	$C_{14}H_{24}O_3$	240

cyclization. In all cases oxidative decomplexation of the HCDC adducts was also realized in order to determine the structure (cf. [3]). This led to the corresponding β-allyloxy-β-ethynyl ketones with yields of 80-90%, and their structures were established on the basis of their PMR and mass spectra.

Decomplexation of (XIX) gave 3-methyl-3-allyloxyhept-6-en-1-yn-5-one. PMR spectrum (δ, ppm, J, Hz): 6.5 dd (1H), 6.25 dd (1H) and 5.8 dd (1H, J = 17.5, 10.5, and 1.5, CH_2=CH—CO), 5.9 m (1H), 5.3 dq (1H), 5.14 dq (1H) and 4.15 m (2H, J = 17.5, 10.5, and 2, CH_2=CH—CH_2O), 3.0 dd (2H, J_{AB} = 14.5, CH_2), 2.53 s (1H, C—H), 1.58 s (3H, CH_3). Mass spectrum: [M^+ —CH_3] 163.

Similarly, from (XVI) we obtained 3-(3',3'-dimethylallyloxy)hex-1-yn-5-one. PMR spectrum (60 MHz, δ, ppm, J, Hz): 6.2 dd (1H), 5.6 dd (1H) and 5.3 dd (1H, J = 17.5, 10, and 3, CH=CH_2), 4.6 dt (1H, J = 6 and 2, CH—O), 2.95 d (2H, CH_2), 2.51 d (—C≡CH), 2.4 s (3H, CH_3), 1.6 s, 1.5 s, [6H, $C(CH_3)_2$]. Mass spectrum (M^+): 180.

Similarly, from (XX) we obtained 1-ethynyl-1-E-crotyloxy-2-acetylcyclopentane in the form of a mixture of the two stereoisomers in a ratio of 3:1. PMR spectrum (δ, ppm, J, Hz): Main isomer, 5.5 m (2H), 4.0 m (2H) and 1.6 d (3H, J = 7, CH_3CH = $CHCH_2O$), 3.1 t (J = 7, CHC = O), 2.27 s (CH_3CO), 1.6—2.0 m [$(CH_2)_3$]. Mass spectrum: [M^+] 206.

TABLE 4. ^{13}C NMR Spectra of Compounds (XXVIII), (XXXI), and (XXXVI)*

Compound	Signals of bicyclo[3.3.0]octene skeleton							Substituent
	C^1	C^2	C^4	C^5	C^6	C^7	C^8	
(XXVIII a)	53,87	48.11	70,83	187,12	125,29	205,58	38,10	CH_2COMe: 41,93: 196,67; 28,22(29,80);
(XXVIII b)	(46,46)	(49.42)	(79,76)				(39,50)	Me_2 at C^2: 20.22 and 24,16
(XXXI a)	44,62	48,89	70,87	188,25	123,88	208,58	40,16	$CH_2COCH{=}CH_2$: 40.06; 196,87; 137,08; 126,54;
(XXXI b)	(45,40)	(49,47)	(69,78)		(125,35)		53,97	26.30(25,61)
(XXXVI a)	60,86	69.85	88,84	188,83	122,16	205		$CH_2CH_2CH_2CHCOMe$: 23,08; 22,57; 39,65; 47.52; 200; 13.37 (22,79; 22,48; 40.35; 47,52; 200; 13,46)
(XXXVI b)	(59,96)	(70,78)	(88,06)		(121,80)		(52,83)	

*The signals of the minor isomer are given in parentheses; the signals were assigned by means of the data from the spectra with off-resonance proton decoupling.

The cyclization of the complexes (XV-XX), (XXII), and (XXVI) was realized by thermolysis on silica gel (Silpearl, Czech, water content 10-15%) according to the previously developed procedure [7-9]. Typical examples are given below.

1,4-Dimethyl-4-acetonyl-3-oxabicyclo[3.3.0]oct-5-en-7-one (XXIX). To a solution of the HCDC complex of (XVII) (0.35 g, 0.75 mmole) in pentane (20 ml) we added 5 g of silica, after which the solvent was removed on a rotary evaporator at 20°C. The dry powder was then heated at 60°C in an atmosphere of oxygen while the flask was rotated. The reaction was monitored by TLC. After 3 h the product was eluted with ether, the solvent was removed, and the residue was chromatographed in a thin layer of silica gel (40/100). We obtained 140 mg (70%) of a mixture of (XXIXa) and (XXIXb) in a ratio of 1:2. The isomers (XXIXa) and (XXIXb) were separated by TLC (Silpearl, 10:1 ether—hexane). We obtained 30 mg (19%) of (XXIXa) , and 65 mg (42%) of (XXIXb) (R_f 0.49 and 0.47, ether). The characteristics of the compounds are given in Tables 2 and 3.

2,2-Dimethyl-4-acetonyl-3-oxabicyclo[3.3.0]oct-5-en-7-one (XXVII). To a solution of (XVI) (0.75 g, 1.6 mmoles) in hexane (30 ml) we added 10 g of silica gel (5/40). The solvent was removed on a rotary evaporator, and the dry powder was heated in an atmosphere of oxygen at 65°C. After 2 h the products were eluted with ether, the solvent was removed, and the residue was separated on silica gel (40/100) in ether. We obtained 185 mg (53%) of (XXVIIIa, b) (ratio 2:3, PMR), R_f 0.52 (ether), and also 70 mg (21%) of (XXXV), R_f 0.3 (ether) and 60 mg (18%) of (XXXIII), R_f 0.39 (ether) (Scheme 6). The characteristics of (XXVIII) are given in Tables 2-4.

Compound (XXXIII). PMR spectrum (δ, ppm, J, Hz): 7.55 and 6.61, two dd (J_{AB} = 17 E-C<u>H</u>=C<u>H</u>=CO), 6.45 s (C=C<u>H</u>CO), 3.24 m, 2.6 dd and 2.25 dd (ABX, J_{AB} = 19, J_{AX} = 7.5, J_{BX} = 2, C<u>H</u>—C<u>H</u>$_2$), 2.37 s (<u>Me</u>CO), 1.3 s and 1.1 s (<u>Me</u>$_2$C).

Compound (XXXV). PMR spectrum (δ, ppm, J, Hz): 5.92 s (C=C<u>H</u>CO), 3.0 and 2.5 dd and 2.08 d (ABX, J_{AB} = 19, J_{AX} = 7, J_{BX} = 2 (C<u>H</u>—C<u>H</u>$_2$), 2.8 m (COC<u>H</u>$_2$C<u>H</u>$_2$C=CH), 2.15 s (MeCO), 1.3 s and 1.08 s (Me_2C).

By the cyclization of (XV) under analogous conditions we obtained the bicyclic product (XXVII) (for its characteristics, see Tables 2 and 3) and also the monocyclic products (XXXII) (26%) and (XXXIV) (26%).

Compound (XXXII). PMR spectrum (δ, ppm, J, Hz): 7.5 and 6.75, two d (J_{AB} = 17, E-C<u>H</u>=C<u>H</u>CO), 6.35 s, (C=C<u>H</u>CO), 3.87 m (AB part of ABX system, J_{AB} = 15.5, J_{AX} = J_{BX} = 4, C<u>H</u>$_2$OH), 2.9 m (C<u>H</u>Me$_2$ and C<u>H</u>—CH$_2$), 2.5 dq (J_1 = 7.5, J_2 = 2, C<u>H</u>Me), 1.22 d, (C<u>H</u>$_3$CH) and 1.25 d (<u>Me</u>$_2$CH).

Compound (XXIV). PMR spectrum (δ, ppm, J, Hz): 5.93 s (C=C<u>H</u>CO), 3.9 m (AB part of ABX system, J_{AB} = 15, J_{AX} = J_{BX} = 4) 2.88 s (C<u>H</u>CH$_2$), 2.7, sept (J = 7, C<u>H</u>Me$_2$), 2.8 and 2.5 m (C<u>H</u>$_2$—C<u>H</u>$_2$), 2.35 dq (J_1 = 7.5, J_2 = 2.5, C<u>H</u>Me), 1.15 d (<u>Me</u>$_2$CH).

The acetates (XXXIIa) and (XXXIIIa) were obtained by the treatment of (XXXII) and (XXXIII) with a mixture of acetic anhydride and triethylamine in the presence of 4-dimethylaminopyridine (yield 85-90%). The characteristics of the acetates are given in Table 3.

TABLE 5. ^{1}H NMR Spectra (δ, ppm, J, Hz) of the Tricyclic Derivatives (XXXVI-XLII)*

Compound	H^1	$2H^2$†	H^7	H^8	Substituent	
					Me at C^8	R at C^7
(XXXVI) ‡	3,0 m	4,2 m 3,3 m	6,0 d(2,5)	2,3 m	1,22 d(7)	3,0 m 2,18 s(R=Me)
(XXXVII)	2,7 m	3,6 t 2,4 t(8)	5,82 d (2,5)	2,1 m	—	3,0m, 2, m 1,0 t(R=Et)
(XXXVIII)	2,6 m	4,24 dd and 3,5 dd	5,78 d (2,5)	2; 2 ddm	—	3,5 m 6,1 dq, 6,82 dq 1,88 d (12,5; 7,5) (R=CH=CHMe)
(XXXIX a)	3,05 m	3,65 t 2,65 dd	5,72 d (2,5)	2,15 m	—	2,5 t 2,2 t 1,8 m 0,9 d(7) ($R=CH_2CHMe_2$)
(XXXIX b)	2,8 m	3,7 t 2,7 dd	5,92 d (2,0)	2,0 m	—	3,0 t 2,4m, 0,92d and 0,91 d(7) ($R=CH_2CHMe_2$)
(XL)	2,9 m	3,6 t и 2,75 dd	6,1 d(2,0)	2,1 m	—	3,97 dd (7; 14), 2,1 m 0,9 t (7) (R=Et)
(XLI a)	2,8 m	3,75 t 2,65 dd	6,2 d(2)	2,1 m	—	3,05 dd (7; 12), 2,1 m 0,8 d (7) ($R=CH_2CHMe)_2$
(XLII)	3,0	4,2 t 3,3 dd	6,05 d	2.2 m	1,2 d(7)	2,8 dd (6; 11); 6,85m, 6,2 m 1,9 d 7) (R=CH=CHMe)

*The spectra of (XXXVI-XXXVIII), (XL), and (XLII) contained a set of signals for the minor isomer. The signals were assigned on the basis of the data from (^{1}H—^{1}H) double resonance for (XXXIXa, b) and (XLIa). In all cases signals for the CH_2 groups of the cyclic aliphatic residue were observed in the region of 1.5-2.0.

†In all cases these protons appear as the AB part of an ABX system with $J_{AB} = J_{AX} = 7$-8 Hz and $J_{BX} = 11$-12 Hz.

‡The spectra of (XXXVII), (XL), and (XLIa) were recorded in hexadeuterobenzene, and those of the other compounds were recorded in deuterochloroform.

The cyclization of the complexes (XXI), (XXIII—XXV) was realized by the method of thermolysis in solution [6]. A typical experiment is given below.

Cyclization of the HCDC Complex (XXIIIa) (Scheme 8). A solution of the complex (XXIIIa) (0.27 g, 0.5 mmole) in petroleum ether (40-70°C, 20 ml) was placed in an airtight steel tube (volume 70 ml) and heated at 60°C for 8 h. The contents were filtered through a layer of aluminum oxide, the solvent was removed, and the residue was separated by preparative TLC (3:1 ether—hexane). We obtained 62 mg (45%) of the product (XXXIXa) ($R_f = 0.37$, Silufol, 3:1 ether—hexane).

For the characteristics of the tricyclic products (XXXV—XLII), see Tables 3-5.

CONCLUSIONS

A short general scheme was developed for the synthesis of a series of bi- and tricyclic compounds containing a 3-oxa-bicyclo[3.3.0]octane fragment on the basis of the successive acylallyloxylation of the double bond in the hexacarbonyldicobalt complexes of conjugated enynes and subsequent intramolecular [2+2+1]-cycloaddition.

LITERATURE CITED

1. W. A. Smit, A. A. Schegolev, A. S. Gybin, et al., Synthesis, 887 (1984).
2. G. Mikaelyan, A. S. Gybin, and W. A. Smit, Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2277 (1985).
3. S. G. Davies, Organotransition Metal Chemistry: Application in Organic Synthesis, Pergamon, New York (1982), p. 512.
4. P. L. Pauson, Tetrahedron, 41, 5855 (1985).

5. N. E. Schore and M. J. Knudsen, J. Org. Chem., 52, 569 (1987).
6. D. C. Billington and D. Willison, Tetrahedron Lett., 25, 4041 (1984).
7. G. S. Mikaelyan and W. A. Smit, Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 2652 (1984).
8. W. A. Smit, A. S. Gybin, S. O. Simonyan, et al., Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 2651 (1985).
9. W. A. Smit, A. S. Gybin, A. S. Shashkov, et al., Tetrahedron Lett., 27, 1241 (1986).
10. G. S. Mikaelyan, W. A. Smit, A. S. Batsanov, and Yu. T. Struchkov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 2105 (1984).
11. W. A. Smit, S. O. Simonyan, A. S. Shashkov, et al., Izv. Akad. Nauk SSSR, Ser. Khim., No. 1, 235 (1987).

STEREOCHEMISTRY OF THE REMOTE OXIDATIVE CYANATION OF METHYLCYCLOHEXANONES

É. I. Troyanskii, V. V. Mizintsev, V. V. Samoshin, A. I. Lutsenko, V. A. Svyatkin, and G. I. Nikishin

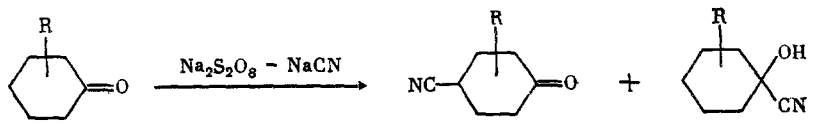
UDC 541.63:542.97:547.594.3

Remote oxidative functionalization, which is based on the rearrangements of heterocentered radicals with migration of hydrogen, represents an effective method for the directed modification of organic compounds at an inactivated carbon atom [1, 2]. Recently we showed that alkanones and alkanals are converted by the action of the $Na_2S_2O_8$—NaCN system in water into γ- or γ- and δ-cyanoalkanones or cyanoalkanoic acids as a result of single-stage remote oxidative cyanation [3]. Earlier these compounds were obtained by the oxidative rearrangement of the cyanohydrins of the respective carbonyl compounds [4, 5].

If the $Na_2S_2O_8$—NaCN system is used, 4-cyanocyclohexanones, which cannot be obtained by the oxidative rearrangement of the cyanohydrin of 1-cyano-1-cyclohexanol [6], is formed regiospecifically from cyclohexanone [3]. The direct cyanation of cyclohexanone to 4-cyanocyclohexanone is a rare example of remote oxidative functionalization, during which the activator (the C=O group) and the carbon atom undergoing functionalization are situated in the same six-membered ring.

In the present work in the development of this new remote functionalization reaction we investigated the regio- and diastereoselectivity of the oxidative cyanation of methylcyclohexanones.

We established that 2-, 3-, and 4-methylcyclohexanones (Ia-c) undergo regiospecific oxidative cyanation at the C^4 atom under the influence of the $Na_2S_2O_8$—NaCN system with two mole equivalents of $Na_2S_2O_8$ and one mole equivalent of sodium cyanide at 80-90°C with the formation of 2-, 3-, or 4-methyl-4-cyanocyclohexanones (IIa-c). The cyanohydrins of the initial ketones (IIIa-c) are formed in addition to (IIa-c).



(Ia-c) (IIa-c) (IIIa-c)

R = 2-Me (a), 3-Me (b), 4-Me (c).

The oxidative cyanation of 2- and 3-methylcyclohexanones (Ia, b) takes place trans-diasteroselectively; cis- and trans-(IIa, b) are formed in ratios of 1:1.5 and 1:2 respectively (Table 1).

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 344-351, February, 1989. Original article submitted September 1, 1987.

 0568-5230/89/3802-0294$12.50