Reactions of nitrogenous derivatives of substituted salicylaldehydes with cyclic ketones and enamines

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The reactions of aminals, the Mannich bases, and azomethines derived from substituted salicylaldehydes were studied. Derivatives of tetrahydrocyclopenta[*b*]- and hexahydrocyclohepta[*b*]chromenes and substituted 2,2′-spirobichromenes were prepared from aminals, and substituted hexahydroxanthenes were synthesized from the Mannich bases. Azomethine derivatives of 5-nitrosalicylaldehyde and aliphatic amines react with cyclohexanone to form 4a-amino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthenes. 4a-Morpholino-7-nitro-9-phenylethynyl-1,2,3,4,9,9a-hexahydroxanthene was studied by X-ray diffraction analysis.

Key words: aminals, azomethines, Mannich bases, substituted salicylaldehydes, quinomethides, cyclic ketones, enamines, cycloaddition, 2*H*-chromenes, 2,2′-spirobichromenes, tetrahydroxanthenes, hexahydroxanthenes.

We have recently[1] reported that aminals of substituted salicylaldehydes react readily with cyclohexanone to form tetrahydroxanthene derivatives. It turned out that other cyclic ketones can react similarly. For example, 3,5-dichlorosalicylaldehyde aminal **1a** and cyclopentanone (**2a**) produced 3a-morpholino-5,7-dichloro-1,2,3,3a-tetrahydrocyclopenta[*b*]chromene (**3**).

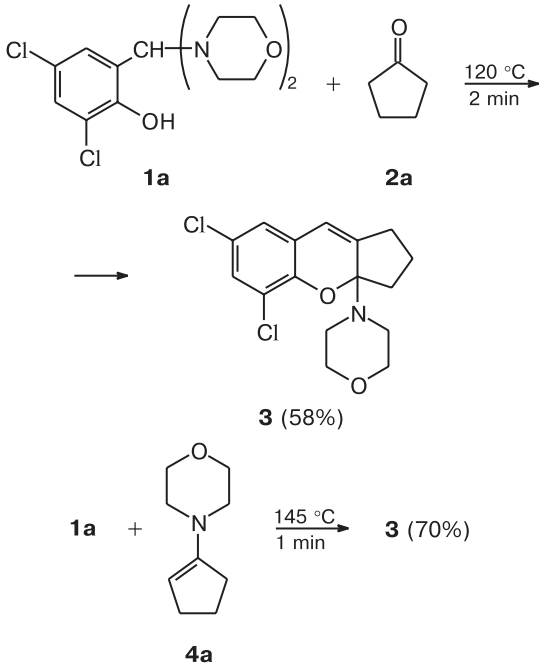
The mechanism of these reactions assumes the concerted formation of *o*-quinomethide from aminal **1a** and of enamine from ketone **2a** and their [4+2]-cycloaddition.[1] In fact, heating of the presynthesized 1-morpholinocyclopentene (**4a**) and aminal **1a** affords chromene **3** (Scheme 1).

3,5-Dichloro- and 3,5-dibromosalicylaldehyde aminals **1a,b** react with cycloheptanone (**2b**) to form hexahydrocyclohepta[*b*]chromenes **5a,b** (Scheme 2).

Chromene **5a** exhibited an unexpected abnormality, which distinguishes it from both chromene **5b** and all tetrahydroxanthenes prepared previously[1] and in this work. According to the ^{1}H NMR spectroscopic data (Table 1), it exists in a $CDCl_3$ solution as at least two geometric isomers.

Each signal from the C(8)H, C(10)H, and C(11)H protons is duplicated by the signal from the isomer (C(8)H and C(10)H protons are duplicated by downfield doublets, and C(11)H is duplicated by an upfield singlet). The ratio of these isomers is approximately 2 : 1 (see Table 1). We specially used the expression "at least" because the ^{1}H NMR spectrum of chromene **5a** exhibits another set of signals from admixtures, *viz.*, from three aromatic protons, two of which are doublets with virtually the same spin-spin coupling constants as those of

Scheme 1



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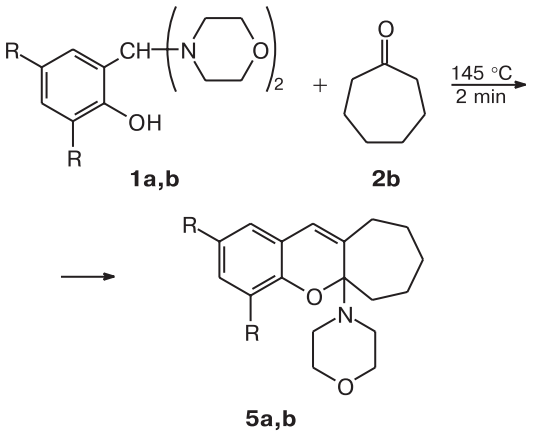
Scheme 2



R = Cl (**a**), Br (**b**)

two main isomers. Diastereomers or *cis*—*trans*-isomers cannot form because compound **5a** contains only one asymmetrical C atom and a rigid double bond in the cycle. The existence of hindered conformers with different geometries of the seven-membered saturated cycle, *i.e.*, conformational isomerism, seems most probable.[2]

The reaction of cycloheptanone (**2b**) and cyclooctanone (**2c**) with 5-nitrosalicylaldehyde aminal **1c**[3] leads to quite different results. The assumed mechanism of this reaction is presented in Scheme 3, and its products are 2,2′-spirobichromenes **10a,b**.

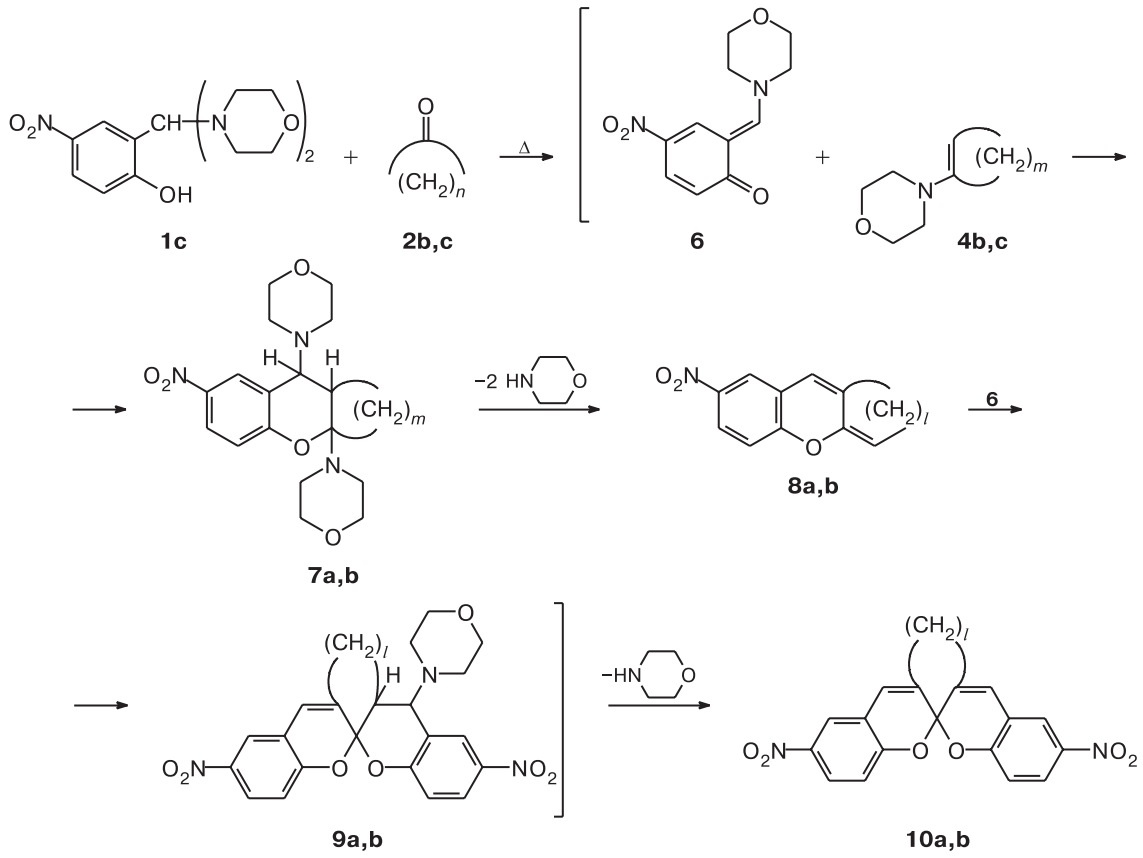
The initial steps in this scheme (up to compounds **8**) are the same as in the mechanism proposed previously[1] for the reaction of aminal **1c** with cyclohexanone, *viz.*, concerted formation of quinomethide **6** and enamines **4**, their cycloaddition, and elimination of two morpholine molecules from tricyclic compounds **7** (the lowest homolog **8** with $l = 3$ was isolated and characterized in the same study[1]). Compounds **8a,b** can be considered as anhydrobases of the corresponding 2,3-cycloalkabenzopyrilium salts. The condensation of such salts with salicylaldehydes followed by treatment with a base is the known method for the synthesis of 3,3′-polymethylene-2,2′-spirobipyrans.[4] In our case, anhydrobases **8** add a

Table 1. Spectral characteristics of compounds **3**, **5**, **10**, **11**, **12**, and **15**

Compound	IR, ν/cm^{-1}	^{1}H ($CDCl_3$), δ (J/Hz)
3	1707 w, 1554 w, 1114 (C—O—C), 941 (cyclopent.)	1.70—2.00 (m, 3 H, $(CH_2)_3$); 2.50 (m, 3 H, $(CH_2)_3$); 2.55 (m, 2 H, CH_2N); 2.78 (m, 2 H, CH_2N); 3.55 (m, 4 H, 2 CH_2O); 6.33 (m, 1 H, C(9)H); 6.85 (d, 1 H, C(8)H, J = 2.3); 7.12 (d, 1 H, C(6)H, J = 2.3)
5a	1560 w (arom.), 1107 (C—O—C)	1.20—4.00 (m, 18 H, 9 CH_2); 6.32 (s, C(11)H); 6.97 (d, C(10)H, J = 2.4); 7.19 (d, C(8)H, J = 2.4) (isomer *1*) and 6.36 (s, C(11)H); 6.81 (d, C(10)H, J = 2.5); 7.10 (d, C(8)H, J = 2.5) (isomer *2*)*
5b	3060 w (CH arom.), 1554 w (arom.), 1114 (C—O—C)	1.35—1.95 (m, 10 H, 5 CH_2); 2.61 (m, 2 H, CH_2N); 2.81 (m, 2 H, CH_2N); 3.57 (m, 4 H, 2 CH_2O); 6.34 (s, 1 H, C(11)H); 6.98 (d, 1 H, C(10)H, J = 2.3); 7.39 (d, 1 H, C(8)H, J = 2.3)
10a	1654, 1607, 1574 (arom.), 1514, 1347 (NO_2)	1.55 (m, 2 H, CH_2); 2.10 (m, 2 H, CH_2); 2.35 (m, 2 H, CH_2); 2.65 (m, 2 H, CH_2); 6.75 (s, 2 H, C(4)H); 6.85 (d, 2 H, C(8)H, J = 8.8); 8.10 (d, 2 H, C(5)H, J = 2.6); 8.05 (dd, 2 H, C(7)H, ^3J = 8.8, ^4J = 2.6)
10b	1667 w, 1647, 1607, 1580 (arom.), 1521, 1347 (NO_2)	1.60 (m, 4 H, 2 CH_2); 1.78 (m, 2 H, CH_2); 2.43 (m, 4 H, 2 CH_2); 6.68 (s, 2 H, 2 C(4)H); 6.89 (d, 2 H, 2 C(8)H, J = 10.0); 8.05 (d, 2 H, 2 C(5)H, J = 2.6); 8.06 (dd, 2 H, 2 C(7)H, ^3J = 10.0, ^4J = 2.6)
11b	3366, 3313 (OH, NH), 1607, 1581, 1548 (arom.), 1514, 1341 (NO_2), 1107 (C—O—C)	2.47 (m, 7 H, Me, 2 CH_2N); 3.64 (t, 4 H, 2 CH_2O, J = 4.4); 5.11 (s, 1 H, CH); 6.90 (m, 3 H, CH arom.); 7.20 (d, 1 H, CH arom., J = 7.85); 7.56 (d, 1 H, CH arom., J = 7.7); 7.88 (dd, 1 H, CH arom., ^3J = 8.95, ^4J = 2.85); 8.22 (br.s, 1 H, CH arom.); 10.86 (s, 1 H, OH); 12.58 (s, 1 H, NH)
12a	2220 w (C≡C), 1614, 1394, 1581 (arom.), 1507, 1341 (NO_2), 1114 (C—O—C)	1.00—1.80 (m, 6 H, 3 CH_2); 2.10 (m, 2 H, CH_2); 2.33 (m, 1 H, C(9a)H); 2.65 (t, 4 H, 2 CH_2N, J = 4.5); 3.58 (m, 4 H, 2 CH_2O); 4.54 (d, 1 H, C(9)H, J = 5.0); 6.87 (d, 1 H, C(5)H, J = 9.0); 7.32 (m, 3 H, CH arom.); 7.48 (m, 2 H, CH arom.); 8.05 (dd, 1 H, C(6)H, ^3J = 9.0, ^4J = 2.75); 8.50 (dd, 1 H, C(8)H, ^4J = 2.75, ^4J = 1.20)
12b	3260 (NH), 1710 w (cyclohex.), 1614, 1581 (arom.), 1514, 1334 (NO_2), 1107 (C—O—C)	1.10—2.10 (m, 9 H, CH_2, CH); 2.54 (s, 3 H, Me); 2.91 (m, 4 H, 2 CH_2N); 3.69 (m, 4 H, 2 CH_2O); 4.41 (d, 1 H, C(9)H, J = 11); 6.72—7.33 (m, 4 H, CH arom.); 6.88 (d, 1 H, C(5)H, J = 9.0)
15	1674 w (C=C), 1614, 1581 (arom.), 1514, 1341 (NO_2)	1.10—2.60 (m, 12 H, 6 CH_2); 2.70 (m, 2 H, CH_2N); 2.90 (m, 2 H, CH_2N); 6.17 (d, 1 H, C(9)H, J = 1.5); 6.68 (d, 1 H, C(5)H, J = 9.0); 7.77 (d, 1 H, C(8)H, J = 3.0); 7.90 (dd, 1 H, C(6)H, ^3J = 9.0, ^4J = 3.0)

* Ratio of isomers ~1 : 2.

Scheme 3



2: n = 6 (**b**), 7 (**c**); **4:** m = 5 (**b**), 6 (**c**); **7:** m = 5 (**a**), 6 (**b**); **8, 9, 10:** l = 4 (**a**), 5 (**b**)

molecule of quinomethide **6** at the double bond conjugated with the 2*H*-chromene structure, after which morpholine is eliminated from intermediate compounds **9**.

It is known[1] that the elimination of morpholine from 4a-morpholino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene is very difficult. It is most likely that analogs with seven- and eight-membered rings eliminate morpholine much more easily, and this explains such a strong difference in the final products.

The Mannich bases derived from salicylaldehyde can reversibly dissociate to *o*-quinomethide and an amine.[5,6] This property allows their use in syntheses of hexahydroxanthene derivatives. The preparation of 2-aminochromones from the Mannich bases (derivatives of phenols and enamines) has been described.[7] We found[3] that brief heating of the Mannich bases **11a,b** with 1-morpholinocyclohexene (**4b**) affords hexahydroxanthenes **12a,b** (Scheme 4). As in the case of aminals, these reactions occur with cyclohexanone (**2d**), *i.e.*, with the formation of enamine **4b** *in situ* (the yields of compounds **12a,b** are 66 and 51%, respectively).

The structure of molecule **12a** was confirmed by X-ray diffraction analysis (Fig. 1, Tables 2 and 3).

The dihydropyran fragment has a distorted sofa conformation. The exit of the C(11) and C(6) atoms from the root-mean-square plane passing through other atoms of the ring (O(1), C(5), C(13), and C(12)) are −0.63 and 0.14 Å, respectively. The cyclohexane and morpholine rings have chair conformations. The exit of the C(10) and C(7), N(2) and O(4) atoms from the root-

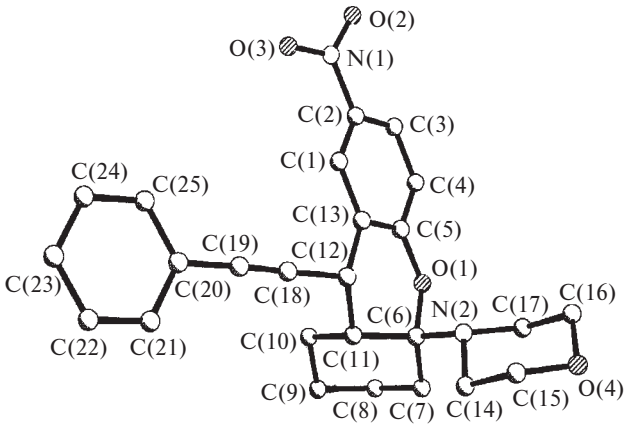
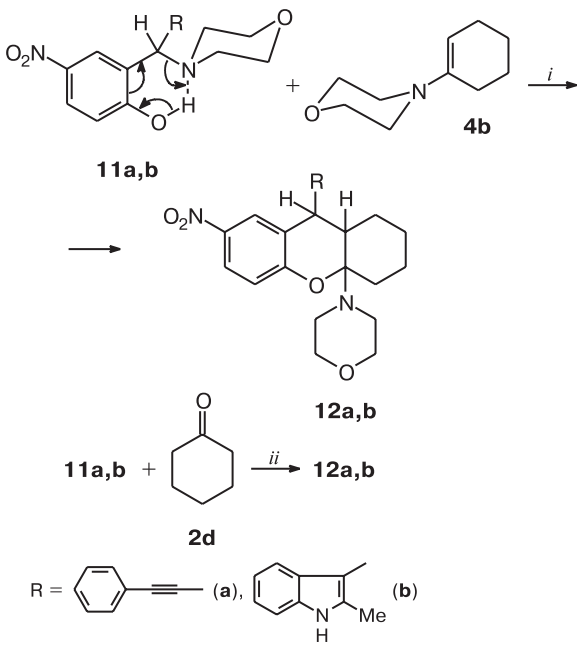


Fig. 1. Structure of molecule **12a**.

Scheme 4



Reagents and conditions: *i*. 150—170 °C, 2 min.
ii. 130—140 °C, 2 min.

mean-square planes passing through other atoms of the rings are –0.66 and 0.63 Å, –0.69 and 0.64 Å, respectively. The dihydropyran and cyclohexane rings are *cis*-fused (torsion angle H(11)—C(11)—C(6)—N(2) 63.6°). The morpholine ring is axially oriented toward the dihydropyran ring (torsion angle C(5)—O(1)—C(6)—N(2) 80.1(2)°), and the substituent

Table 2. Bond lengths (*d*) in molecule **12a**

Bond	*d*/Å	Bond	*d*/Å
N(1)—O(3)	1.243(2)	N(1)—O(2)	1.245(2)
N(1)—C(2)	1.486(3)	N(2)—C(14)	1.486(2)
N(2)—C(17)	1.487(2)	N(2)—C(6)	1.489(2)
O(1)—C(5)	1.381(2)	O(1)—C(6)	1.472(2)
O(4)—C(16)	1.434(2)	O(4)—C(15)	1.438(2)
C(1)—C(2)	1.389(3)	C(1)—C(13)	1.402(2)
C(2)—C(3)	1.398(3)	C(3)—C(4)	1.396(3)
C(4)—C(5)	1.404(3)	C(5)—C(13)	1.427(3)
C(6)—C(7)	1.543(3)	C(6)—C(11)	1.562(2)
C(7)—C(8)	1.536(3)	C(8)—C(9)	1.539(3)
C(9)—C(10)	1.543(3)	C(10)—C(11)	1.548(2)
C(11)—C(12)	1.558(2)	C(12)—C(18)	1.492(2)
C(12)—C(13)	1.536(2)	C(14)—C(15)	1.526(3)
C(16)—C(17)	1.527(3)	C(18)—C(19)	1.201(2)
C(19)—C(20)	1.464(3)	C(20)—C(21)	1.394(3)
C(20)—C(25)	1.394(3)	C(21)—C(22)	1.392(3)
C(22)—C(23)	1.381(3)	C(23)—C(24)	1.377(3)
C(24)—C(25)	1.395(3)		

Table 3. Bond angles (ω) in molecule **12a**

Angle	ω/deg	Angle	ω/deg
O(3)—N(1)—O(2)	123.8(2)	O(3)—N(1)—C(2)	118.4(2)
O(2)—N(1)—C(2)	117.7(2)	C(14)—N(2)—C(17)	108.2(1)
C(14)—N(2)—C(6)	115.6(1)	C(17)—N(2)—C(6)	114.3(1)
C(5)—O(1)—C(6)	119.4(1)	C(16)—O(4)—C(15)	109.6(2)
C(2)—C(1)—C(13)	120.6(2)	C(1)—C(2)—C(3)	121.9(2)
C(1)—C(2)—N(1)	118.9(2)	C(3)—C(2)—N(1)	119.2(2)
C(4)—C(3)—C(2)	118.4(2)	C(3)—C(4)—C(5)	120.5(2)
O(1)—C(5)—C(4)	115.7(2)	O(1)—C(5)—C(13)	123.5(2)
C(4)—C(5)—C(13)	120.8(2)	O(1)—C(6)—N(2)	105.5(1)
O(1)—C(6)—C(7)	104.5(1)	N(2)—C(6)—C(7)	115.3(1)
O(1)—C(6)—C(11)	108.5(1)	N(2)—C(6)—C(11)	111.3(1)
C(7)—C(6)—C(11)	111.1(1)	C(8)—C(7)—C(6)	113.5(2)
C(7)—C(8)—C(9)	111.8(2)	C(8)—C(9)—C(10)	110.7(2)
C(9)—C(10)—C(11)	112.0(2)	C(10)—C(11)—C(12)	113.1(1)
C(10)—C(11)—C(6)	111.6(2)	C(2)—C(11)—C(6)	108.6(1)
C(18)—C(12)—C(13)	113.5(1)	C(18)—C(12)—C(11)	113.9(1)
C(13)—C(12)—C(11)	108.4(1)	C(1)—C(13)—C(5)	117.7(2)
C(1)—C(13)—C(12)	123.5(2)	C(5)—C(13)—C(12)	118.8(2)
N(2)—C(14)—C(15)	110.0(2)	O(4)—C(15)—C(14)	112.5(2)
O(4)—C(16)—C(17)	111.9(2)	N(2)—C(17)—C(16)	109.6(2)
C(19)—C(18)—C(12)	174.9(2)	C(18)—C(19)—C(20)	176.9(2)
C(21)—C(20)—C(25)	117.9(2)	C(21)—C(20)—C(19)	120.1(2)
C(25)—C(20)—C(19)	122.0(2)	C(22)—C(21)—C(20)	121.0(2)
C(23)—C(22)—C(21)	120.4(2)	C(24)—C(23)—C(22)	119.3(2)
C(23)—C(24)—C(25)	120.7(2)	C(20)—C(25)—C(24)	120.7(2)

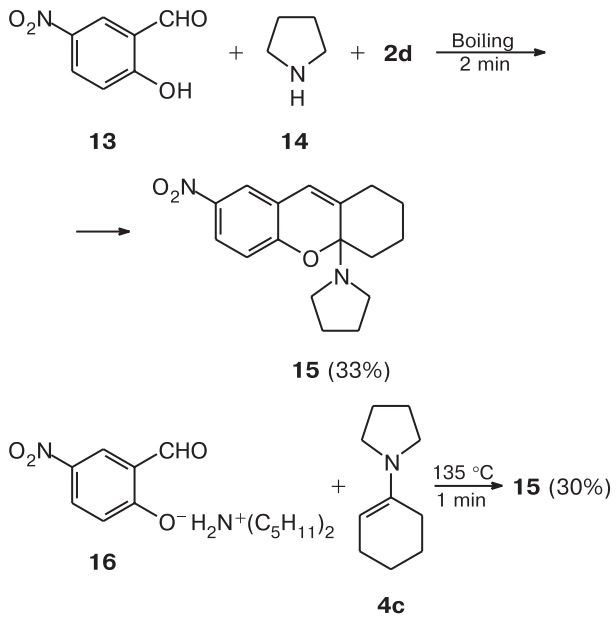
at the C(12) atom is in the equatorial position (torsion angle C(5)—C(13)—C(12)—C(18) 156.4(2)°). The plane of the NO_2 group deviates from the plane of the benzene ring by 11.3(3)°.

Unfavorable nonbonded interactions (shortened intramolecular contacts H(7A)...C(17) 2.75 Å, H(10A)...C(18) 2.79 Å, and H(1)...C(18) 2.65 Å at a sum of van der Waals radii of 2.87 Å)[8] elongate the C(12)—C(13) (1.536(2) Å), C(11)—C(12) (1.558(2) Å), C(12)—C(18) (1.492(2) Å), and N(2)—C(6) (1.489(2) Å) bonds compared to average values of 1.503, 1.513, 1.466, and 1.469 Å, respectively.[9] It can be assumed that the nonequivalent shortened intramolecular H(10A)...C(18) and H(1)...C(18) contacts bend the triple bond (C(12)—C(18)—C(19) and C(18)—C(19)—C(20) angles are 174.9(2) and 176.9(2)°, respectively).

It is known that 5-nitrosalicylaldehyde forms aminal only with morpholine (pK_a = 8.33).[10] Its reaction with strongly basic (pK_a ~11) secondary aliphatic amines affords ion associates.[11] Their anions, like aminals, react with enamines in cycloaddition reactions to form the corresponding tetrahydroxanthenes.[1] Scheme 5 represents the first example of the one-pot synthesis of previously undescribed 7-nitro-4a-pyrrolidino-2,3,4,4a-tetrahydro-1*H*-xanthene (**15**) in which the ion associate and enamine are formed *in situ*. Tetrahydroxanthene **15** was also prepared in the independent synthesis from ion as-

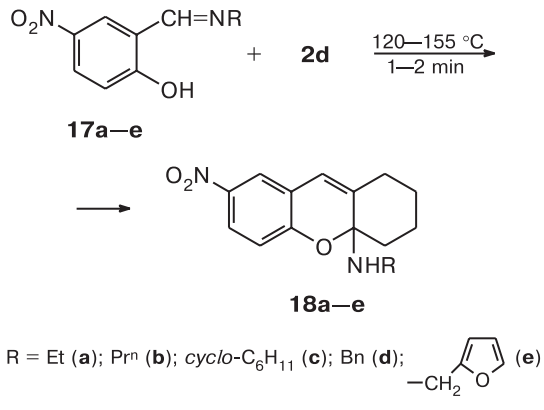
sociate **16** and enamine **4c** using a procedure described earlier[1] (see Scheme 5).

Scheme 5



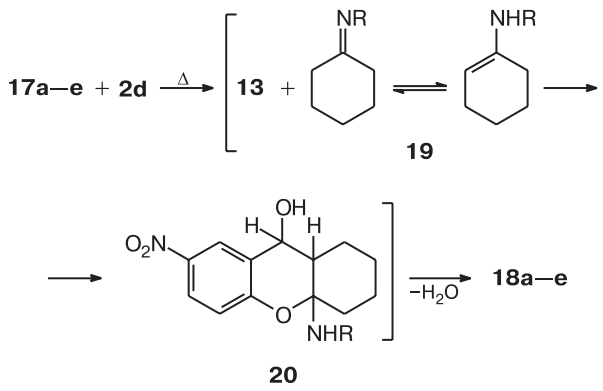
Secondary amines were used in all reactions discussed above. The use of azomethines instead of aminals provides the formation of analogous structures with primary amines as substituents. It has been found[12] that heating of azomethines **17** derived from 5-nitrosalicylaldehyde and aliphatic amines with cyclohexanone (**2d**) produces 4a-amino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthenes **18** (Scheme 6).

Scheme 6



We believe that the first step of this reaction is transamination with the formation of 5-nitrosalicylaldehyde (**13**) and the corresponding cyclohexanone azomethine **19**. The reaction of these compounds (cyclohexanone azomethines in the enamine form) affords hexahydroxanthenes **20**, which are dehydrated to give tetrahydroxanthene derivatives **18** (Scheme 7). The formation of analogs of compound **20** by the condensation of salicylaldehydes with enamines has previously been described.[13]

Scheme 7

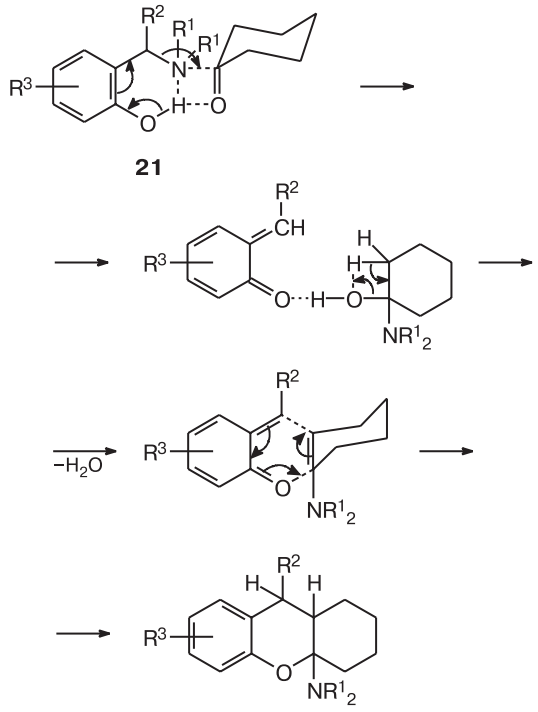


All presented reactions of cyclic ketones can easily be explained by the concerted formation of enamine and *o*-quinomethide and their cycloaddition. The formal scheme assumes the dissociation of aminal or the Mannich base to quinomethide and amine and condensation of the latter with cyclic ketone to form an enamine. The possibility of this dissociation is confirmed by spectroscopic data.[1,5,6] However, it is known that synthesis of enamines takes a long time. This requires boiling of components in toluene for many hours in the presence of acid catalysts and with continuous removal of water that formed.[14]

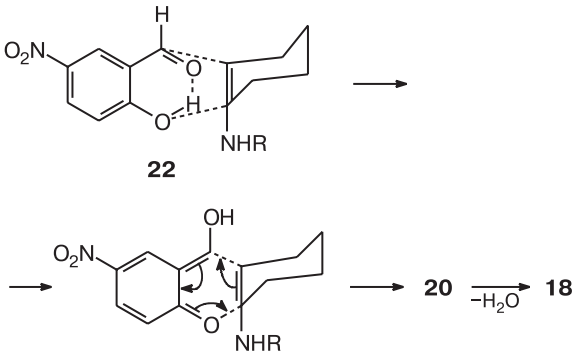
In our cases, the reactions take dozens of seconds, and the yields of final products suggest high degrees of conversion of cyclic ketones and amines to enamines over such short time intervals. These facts suggest that enamine formation and cycloaddition occur, in fact, in the intermediate (or activated) complex formed by the nitrogenous base of the salicylaldehyde derivative and cyclic ketone. The available data on the structure of nitrogen bases[15,16] suggest that complex formation involves cyclic structures with intramolecular hydrogen bonding, which can be considered as an intermediate step of proton transfer.[17] The reaction scheme including such intramolecular acid catalysis is presented below (Scheme 8).

If $R^2 = NR^1_2$, then compound **21** is an aminal complex; if R^2 is an organic radical, then compound **21** is a complex of the Mannich base. We assume that the formation of tetrahydroxanthenes **18** involves the proton transfer to the carbonyl oxygen atom and cycloaddition in a similar complex **22** formed by the cyclic aldehyde structure with the intramolecular hydrogen bond and enamine (Scheme 9).

Scheme 8



Scheme 9



Experimental

IR spectra were recorded on a Specord IR-75 instrument in Nujol. ^{1}H NMR spectra were obtained on a Varian UNITY-300 spectrometer. Aminal **1c** was synthesized according to a previously described procedure.[16] Cycloalkanone enamines were synthesized by known procedures.[14] The spectral parameters of the compounds obtained are presented in Tables 1 and 4.

Synthesis of azomethines 17 (general procedure). 5-Nitrosalicylaldehyde (1.7 g, 0.01 mol) was dissolved in boiling Pr^{i}OH (10 mL), and aliphatic amine (0.11 mol) was added to the hot solution (in the case of azomethine **17a**, gaseous ethylamine was passed through a hot solution). The mixture was cooled, and light petroleum (5 mL) was added. The yellow crystalline precipitate that formed was filtered off, washed with light petroleum, dried in air, and used in syntheses without additional purification. The yields were 90—100%, m.p.: 147—156 °C (**17a**), 114—115 °C (**17b**), 142—143 °C (**17c**), 88—89 °C (**17d**), 120 °C (**17e**).

Table 4. Spectral parameters of tetrahydroxanthenes **18a—e**

Compound	IR, ν/cm^{-1}	^{1}H ($CDCl_3$), δ (J/Hz)
18a	3313 (NH), 1614, 1574 (arom.), 1514, 1341 (NO_2)	0.99 (t, 3 H, Me, J = 7.1); 1.30—2.50 (m, 8 H, 4 CH_2); 2.59 (q, 2 H, CH_2, J = 7.1); 6.25 (s, 1 H, C(9)H); 6.73 (d, 1 H, C(5)H, J = 8.9); 7.88 (d, 1 H, C(8)H, J = 2.7); 7.91 (dd, 1 H, C(6)H, ^3J = 8.9, ^4J = 2.7)
18b	3333 (NH), 1607, 1581 (arom.), 1514, 1334 (NO_2)	0.82 (t, 3 H, Me, J = 7.35); 1.20—2.60 (m, 12 H, 6 CH_2); 6.25 (s, 1 H, C(9)H); 6.73 (d, 1 H, C(5)H, J = 8.9); 7.82 (d, 1 H, C(8)H, J = 2.75); 7.95 (dd, 1 H, C(6)H, ^3J = 8.9, ^4J = 2.75)
18c	3340 (NH), 1607, 1581 (arom.), 1514, 1334 (NO_2)	0.90—2.70 (m, 19 H, CH_2, CH); 6.21 (s, 1 H, C(9)H); 6.72 (d, 1 H, C(5)H, J = 8.9); 7.84 (d, 1 H, C(8)H, J = 2.75); 7.96 (dd, 1 H, C(6)H, ^3J = 8.9, ^4J = 2.75)
18d	3360 (NH), 1607, 1574 (arom.), 1514, 1334 (NO_2)	1.40—2.65 (m, 8 H, 4 CH_2); 3.73 (d, 2 H, CH_2N, J = 9.0); 6.31 (d, 1 H, C(9)H, J = 1.9); 6.76 (d, 1 H, C(5)H, J = 8.9); 7.24 (m, 5 H, Ph); 7.85 (d, 1 H, C(8)H, J = 2.75); 7.97 (dd, 1 H, C(6)H, ^3J = 8.9, ^4J = 2.75)
18e	3350 (NH), 1607, 1574 (arom.), 1507, 1334 (NO_2)	1.40—2.65 (m, 8 H, 4 CH_2); 3.74 (s, 2 H, CH_2N); 5.99 (d, 1 H, furan C(3)H, J = 3.15); 6.21 (m, 1 H, furan C(4)H); 6.30 (d, 1 H, C(9)H, J = 1.85); 6.69 (d, 1 H, C(5)H, J = 8.9); 7.27 (d, 1 H, furan C(5)H, J = 1.85); 7.84 (d, 1 H, C(8)H, J = 2.75); 7.94 (dd, 1 H, C(6)H, ^3J = 8.9, ^4J = 2.75)

5,7-Dichloro-3a-morpholino-1,2,3,3a-tetrahydrocyclopenta[b]chromene (3). ***A.*** 3,5-Dichlorosalicylaldehyde aminal **1a** (0.35 g, 1 mmol) and cyclopentanone **2a** (0.2 mL, 2 mmol) were boiled for 2 min at 110—120 °C. The mixture was cooled, MeOH (3 mL) was added, and the resulting solution crystallized upon cooling with ice. The precipitate was filtered off, washed with cold MeOH, and dried. Chromene **3** (0.24 g, 58%) was obtained as colorless crystals with m.p. 135—137 °C (from MeOH).

B. A mixture of aminal **1a** (0.35 g, 1 mmol) and 1-morpholinocyclopentene **4a** (0.3 mL, 2 mmol) was heated to 145 °C and cooled. MeOH (3 mL) was added to the mixture, which was then processed as described above. Chromene **3** (0.23 g, 70%) was obtained as colorless crystals with m.p. 135—137 °C (from MeOH). Found (%): C, 58.98; H, 5.16; Cl, 21.22; N, 4.35. $C_{16}H_{17}Cl_2NO_2$. Calculated (%): C, 58.91; H, 5.25; Cl, 21.74; N, 4.29.

7,9-Dichloro-5a-morpholino-1,2,3,4,5,5a-hexahydrocyclohepta[b]chromene (5a). A mixture of aminal **1a** (1.05 g, 3 mmol)

and cycloheptanone **2b** (0.6 mL, 5 mmol) was heated for 2 min at 140—145 °C. After cooling MeOH (5 mL) was added, and the mixture was cooled with ice and scratched with a glass rod. After storing on ice for 1 h, the crystals that formed were filtered off, washed with cold MeCN and hexane, and dried. Chromene **5a** (0.5 g, 47%) was obtained as colorless crystals with m.p. 125 °C (from MeCN). Found (%): C, 60.52; H, 5.64; Cl, 20.69; N, 3.71. $C_{18}H_{21}Cl_2NO_2$. Calculated (%): C, 61.03; H, 5.97; Cl, 20.01; N, 3.95.

7,9-Dibromo-5a-morpholino-1,2,3,4,5,5a-hexahydrocyclohepta[*b*]chromene (5b). A mixture of aminal **1b** (2.6 g, 6 mmol) and cycloheptanone **2b** (1 mL, 8 mmol) was boiled for 2 min at 135 °C, and MeOH (15 mL) was added after cooling. The mixture was cooled with ice and scratched with a glass rod to complete solidification. The precipitate was filtered off, washed repeatedly with cold MeOH, and dried. The yield of the crude product was 1.8 g. Recrystallization from Pr^iOH (40 mL) gave 1 g (39%) of chromene **5b** as colorless crystals with m.p. 132—135 °C. Found (%): C, 49.15; H, 4.65; Br, 36.72; N, 3.27. $C_{18}H_{21}Br_2NO_2$. Calculated (%): C, 48.78; H, 4.78; Br, 36.06; N, 3.16.

3,3´-Tetramethylene-6,6´-dinitro-2,2´-spirobichromene (10a). A mixture of aminal **1c** (0.65 g, 2 mmol) and cycloheptanone **2b** (0.4 mL, 3.4 mmol) was heated for 2 min at 125—130 °C. After cooling 3 mL of MeOH were added, and the mixture was worked up as described for compound **3**. The yield was 0.16 g (41%). After recrystallization from MeCN (20 mL), spirobichromene **10a** was obtained as colorless crystals with m.p. 292—295 °C. Found (%): C, 64.11; H, 3.95; N, 7.48. $C_{21}H_{16}N_2O_6$. Calculated (%): C, 64.28; H, 4.11; N, 7.14.

3,3´-Pentamethylene-6,6´-dinitro-2,2´-spirobichromene (10b). Aminal **1c** (0.65 g, 2 mol) was added to the melt of cyclooctanone (**2c**) (0.35 g, 2 mmol), and the resulting mixture was heated for 2 min at 120 °C. After cooling, 5 mL of MeOH were added, and the mixture was cooled with ice and scratched with a glass rod. The precipitate was filtered off, washed with MeOH, and dried. Spirobichromene **10b** was obtained in 34% yield (0.14 g) as colorless crystals with m.p. 295—305 °C (from MeCN). Found (%): C, 64.70; H, 4.60; N, 7.20. $C_{22}H_{18}N_2O_6$. Calculated (%): C, 65.02; H, 4.46; N, 6.85.

2-Methyl-3-[morpholino(2-hydroxy-5-nitrophenyl)methyl]indole (11b). A mixture of aminal **1c** (0.65 g, 2 mmol) and 2-methylindole (0.52 g, 4 mmol) was ground in a mortar and melted at 110 °C whereupon a new crystalline precipitate rapidly formed. After cooling, 3 mL of MeCN were added, and the mixture was cooled with ice and washed with cold MeCN and hexane. Compound **11b** was obtained in 84% yield (0.62 g) as light yellow crystals with m.p. 220—225 °C (from MeCN). Found (%): C, 65.50; H, 5.45; N, 11.32. $C_{20}H_{21}N_3O_4$. Calculated (%): C, 65.38; H, 5.76; N, 11.44.

4a-Morpholino-7-nitro-9-phenylethynyl-1,2,3,4,4a,9a-hexahydroxanthene (12a). ***A.*** A mixture of amine **11a** [16] (0.67 g, 2 mmol) and 1-morpholinocyclohexene (**4b**) (0.8 mL, 5 mmol) was heated for 2 min at 150—155 °C, and Pr^iOH (8 mL) was added after cooling. The mixture was cooled with ice and scratched with a glass rod, and the precipitate that formed was filtered off and washed with cold Pr^iOH and light petroleum. Compound **12a** (0.29 g, 36%) was obtained as light yellow crystals with m.p. 190—192 °C (from MeCN).

B. A mixture of amine **11a** (1 g, 3 mmol) and cyclohexanone (**2d**) (0.8 mL, 7 mmol) was heated for 2 min to 130—140 °C, and MeOH (16 mL) was added after cooling. The mixture was cooled with ice and scratched with a glass rod. The light yellow crystalline precipitate was filtered off, washed with cold MeOH, and dried. The yield of the crude product was 66% (0.82 g). After recrystallization from MeOH (25 mL), a colorless substance with m.p. 190—193 °C was obtained. Found (%): C, 71.67; H, 6.89; N, 6.95. $C_{25}H_{26}N_2O_4$. Calculated (%): C, 71.75; H, 6.26; N, 6.69.

9-(2-Methylindol-3-yl)-4a-morpholino-7-nitro-1,2,3,4,4a,9a-hexahydroxanthene (12b). ***A.*** A mixture of the Mannich base **11b** (0.45 g, 1.2 mmol) and 1-morpholinocyclohexene (**4b**) (0.9 mL, 5 mmol) was heated for 2 min at 165—170 °C and cooled to ~50 °C, and 4 mL of CCl_4 were added. The mixture was scratched with a glass rod, and hexane (4 mL) was added. The precipitate was filtered off, washed with hexane, and dried. Compound **12b** (0.45 g, 82%) was obtained as colorless crystals with m.p. 227—230 °C.

B. A mixture of compound **11b** (1 g, 2.7 mmol) and cyclohexanone (**2d**) (0.8 mL, 8 mmol) was heated at 130—135 °C to complete homogenization and cooled to 70—80 °C. MeOH (5 mL) was added, and the mixture was boiled until a crystalline precipitate formed (2—3 min). The mixture was cooled and filtered. The precipitate was cooled with cold MeOH and dried. Compound **12b** (0.62 g, 51%) was obtained as colorless crystals with m.p. 227—230 °C (from MeOH). Found (%): C, 69.48; H, 6.00; N, 9.73. $C_{26}H_{29}N_3O_4$. Calculated (%): C, 69.78; H, 6.53; N, 9.39.

7-Nitro-4a-pyrrolidino-2,3,4,4a-tetrahydro-1*H*-xanthene (15). ***A.*** A mixture of 5-nitrosalicyladehyde (**13**) (1.67 g, 10 mmol) and pyrrolidine (**14**) (1 mL, 12 mmol) was heated to dissolution, cyclohexanone (**2d**) (1.5 mL, 14 mmol) was added, and the mixture was boiled for 2 min. The reaction mixture was dissolved in $CHCl_3$ and passed through a column with Al_2O_3. The solvent was evaporated, and a light yellow oil was crystallized on cooling with ice and trituration with hexane. The precipitate was filtered off, washed with hexane, and dried. Compound **15** was obtained in 33% yield (0.7 g) with m.p. 106—108 °C (from a Pr^iOH—hexane (1 : 1) mixture).

B. A mixture of ion associate **16** [11] (0.66 g, 2 mmol) and 1-pyrrolidinocyclohexene (**4c**) (0.8 mL, 4 mmol) was heated for 1 min at 135 °C and cooled. MeOH (10 mL) was added, and the mixture was poured into 50 mL of cold water. The precipitate was filtered off, washed with 50% EtOH, and dried. The yield of the crude product was 0.3 g. Recrystallization from Pr^iOH gave compound **15** (0.18 g, 30%) as yellow crystals with m.p. 106—108 °C. Found (%): C, 67.50; H, 6.45; N, 9.62. $C_{17}H_{20}N_2O_3$. Calculated (%): C, 67.98; H, 6.71; N, 9.33.

4a-Ethylamino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene (18a). A mixture of azomethine **17a** (0.4 g, 2 mmol) and cyclohexanone (**2d**) (0.4 mL, 4 mmol) was heated for 2 min at 110—120 °C and cooled, and water (0.5 mL) was added. The oil that formed crystallized after cooling with ice and trituration. The precipitate was filtered off and recrystallized from hexane. The yield was 0.35 g (63%).* Double recrystallization from MeOH gave colorless crystals with m.p. 104—105 °C. Found (%): C, 65.31; H, 6.24; N, 10.57. $C_{15}H_{18}N_2O_3$. Calculated (%): C, 65.68; H, 6.61; N, 10.21.

* The substance contains an insignificant amount of a colored admixture, which confers a reddish color to the substance.

4a-Propylamino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene (18b). A mixture of azomethine **17b** (0.21 g, 1 mmol) and cyclohexanone (**2d**) (0.2 mL, 2 mmol) was boiled for 1 min at ~140 °C, cooled, and passed through a column with Al_2O_3 (eluent $CHCl_3$), The solvent was evaporated and the oily residue crystallized upon trituration. Compound **18b** was obtained in 79% yield (0.23 g) with m.p. 95 °C (from hexane). Found (%): C, 66.19; H, 6.75; N, 9.37. $C_{16}H_{20}N_2O_3$. Calculated (%): C, 66.65; H, 6.99; N, 9.72.

4a-Cyclohexylamino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene (18c). A mixture of azomethine (**17c**) (0.5 g, 2 mmol) and cyclohexanone (**2d**) (0.4 mL, 4 mmol) was boiled for 2 min at 145—155 °C. After cooling, 2 mL of MeOH were added, and the mixture was cooled with ice and scratched with a glass rod. The precipitate that formed was filtered off and recrystallized from hexane (10 mL) and MeOH (in ice). The precipitated was filtered off, washed with cold MeOH, and dried. Compound **18c** was obtained in 30% yield (0.2 g) as colorless crystals with m.p. 113—115 °C. Found (%): C, 69.12; H, 7.60; N, 8.32. $C_{19}H_{24}N_2O_3$. Calculated (%): C, 69.49; H, 7.37; N, 8.53.

4a-Benzylamino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene (18d). A mixture of azomethine **17d** (0.52 g, 2 mmol) and cyclohexanone (**2d**) (0.4 mL, 4 mmol) was heated for 2 min at 110—120 °C. After cooling 2 mL of MeOH were added, and the mixture was triturated. The precipitate that formed was filtered off, washed with cold MeOH, and dried. The yield of the crude product was 0.5 g. Recrystallization from MeOH (25 mL) gave compound **18d** (0.35 g, 51%) as pale-yellow crystals with m.p. 113—115 °C. Found (%): C, 71.94; H, 6.24; N, 8.21. $C_{20}H_{20}N_2O_3$. Calculated (%): C, 71.41; H, 5.99; N, 8.33.

4a-Furylamino-7-nitro-2,3,4,4a-tetrahydro-1*H*-xanthene (18e). A mixture of azomethine **17e** (2.46 g, 10 mmol) and cyclohexanone (**2d**) (2 mL, 19 mmol) was heated to boiling (~135 °C) and boiled for 1 min. After cooling MeOH (10 mL) was added, and the mixture was heated to homogenization, cooled with ice, and triturated. The light crystalline precipitate that formed was filtered off, washed with cold MeOH, and dried. The yield was 2.32 g (71%). Recrystallization from 15 mL of EtOH gave 2.1 g of light yellow crystals with m.p. 90—95 °C. Repeated crystallization from 20 mL of MeOH gave 1.8 g of compound **18e** as light yellow crystals with m.p. 95—97 °C. Found (%): C, 66.53; H, 5.48; N, 8.71. $C_{18}H_{18}N_2O_4$. Calculated (%): C, 66.25; H, 5.56; N, 8.58.

X-ray diffraction analysis of compound 12a. Crystals **12a** are monoclinic ($C_{25}H_{26}N_2O_4$), at 20 °C a = 12.387(4) Å, b = 11.549(3) Å, c = 16.296(5) Å, β = 102.65°, V = 2274.7(12) Å^3, M = 418.48, Z = 4, space group $P2_1/n$, d_{calc} = 1.222 g cm^{-3}, μ(Mo-Kα) = 0.083 mm^{-1}, F(000) = 888. Unit cell parameters and intensities of 4199 reflections were measured on a Siemens P3/PC automated four-circle diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scan mode, $2\theta_{max}$ = 50°). The structure was solved by the direct method using the SHELXTL PLUS program package.[18] Positions of H atoms were calculated geometrically and refined using the riding model ($U_i = 1.2U_{eq}$ of the atom bound to the specific hydrogen atom). The structure was refined by F^2 using the full-matrix least-squares method in the anisotropic approximation to wR_2 = 0.098 from 4002 reflections (R_1 = 0.044 from 2018 reflections with $F > 4\sigma(F)$, S = 0.953).

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