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Synthetic Utilization of Polynitroaromatic Compounds. 3. Preparation of Substituted Dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones from 2,4,6-Trinitrobenzoic Acid via Nucleophilic Displacement of Nitro Groups

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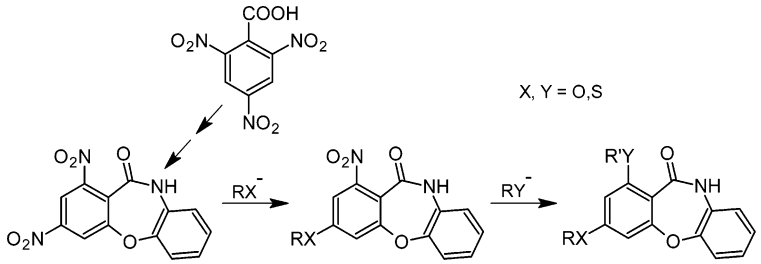
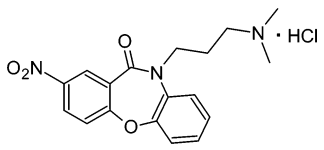


1,3-Dinitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one, prepared by intramolecular displacement of nitro group in *N*-(2-hydroxyphenyl)-2,4,6-trinitrobenzamide, reacts with O- and S-nucleophiles to yield the products of mono- or bis-substitution of the nitro groups. The nitro group in position 3 is displaced first. This observation is in contrast with earlier results for the nitro-substituted benzoannulated five-membered heterocycles. This difference in reactivity is likely due to the increased steric hindrance for *peri*-nitro group displacement in the case of the benzoannulated seven-membered heterocycle. N-Alkylation of the nitro-substituted dibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-ones yields analogues of a known antidepressant drug Sintamil. The structure of the products is confirmed by NOE experiments and alternative synthesis.

Introduction

Dibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-ones are known to display various kinds of biological activity.[1,2] In particular, 10-[3-(dimethylamino)propyl]-2-nitrodibenz[*b*,*f*][1,4]-oxazepin-11(10*H*)-one (Sintamil) is an efficient antidepressant.[3,4]



Sintamil

Therefore, in the process of our work aimed at utilization of aromatic polynitrocompounds,[5−7] these heterocycles drew our attention as attractive synthetic targets. Dibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-ones could be accessed by an intramolecular cyclization of 2-hydroxyanilides of ortho-substituted benzoic acids (X = Cl, F)[8−10] (usually, the presence of an additional electron-withdrawing sub-

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(9) Nagarajan K.; Venkateswarlu A.; Kulkarni C. L.; Shah R. K. *Indian J. Chem*. **1974**, *12*, 227.
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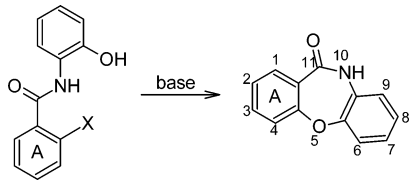
SCHEME 1



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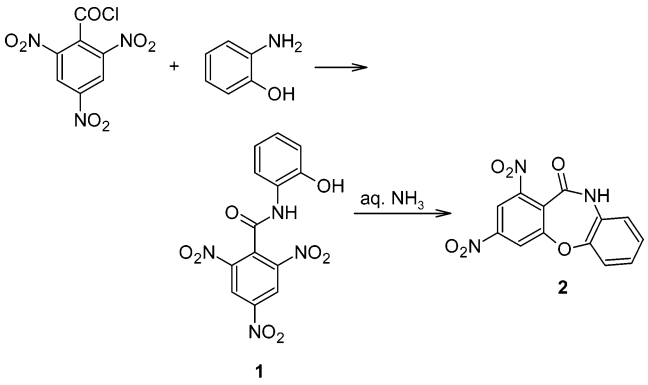

stituent in the A ring is needed; Scheme 1). In this respect, we were interested in utilization of an S_NAr of the nitro group for the construction of the targeted seven-membered ring systems. This reaction has been successfully applied to the synthesis of several heterocyclic systems.[11,12]

Results and Discussion

In this article we report the synthesis of dibenz[*b*,*f*]-[1,4]oxazepin-11(10*H*)-ones containing various substituents in positions 1 and 3 from 2,4,6-trinitrobenzoic acid (prepared, in turn, by oxidation of TNT with dilute HNO_3[6]). The acid was converted to the corresponding acid chloride, followed by its conversion to *o*-hydroxyanilide **1**. Compound **1** underwent an intramolecular nucleophilic displacement of the nitro group in mild conditions upon treatment with base (aqueous NH_3) to yield 1,3-dinitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one **2** (Scheme 2).[13] Subsequently, we found that the nitro groups in compound **2** (one or both) could undergo nucleophilic displacement to afford products **3** and **4** (Scheme 3). A series of O- and S-nucleophiles including alcohols, phenols, thiols, and thiophenols were found to be reactive. The first nitro group is displaced under relatively mild conditions (65−100 °C). The substitution of the second function required higher temperatures, specifically, 100−120 °C for thiols and thiophenols and 140−150 °C for phenols (Tables 1 and 2). For instance, reaction of compound **2** with 2 equiv of guaiacol at 120 °C resulted exclusively in a product of monosubstitution **3k** (Table 1). For alcohols, the corresponding products of bis-substitution **4** were not detected.

A number of primary alcohols ROH yielded the substitution products (R = Me, Et, Pr, Bn, $HO(CH_2)_2$), whereas secondary alcohols (*i*-PrOH, cyclohexanol) did not afford the expected **3** and **4**. Phenols with both electron-donating and electron-withdrawing substituents reacted smoothly.

Regioselectivity of the nucleophilic substitution in 1,3-dinitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one **2** was further studied by NOE experiments (Scheme 4). For example, irradiation of the methoxy group signal (δ 3.80) in **4e** caused an increase of intensity for the H(2) and H(4) signals (δ 6.82 and 6.72, respectively), whereas upon irradiation of SCH_2 group signal (δ 4.18) intensities of H(2) (δ 6.82) and *ortho*-phenyl (δ 7.38) proton signals were increased. In the 2D NOESY spectrum of **4c**, we observed two cross-peaks between the signals of SCH_2 (δ 2.94) and aromatic protons H(2) and H(4) (δ 6.60 and 7.08, respectively). In addition, a cross-peak between the

SCHEME 3

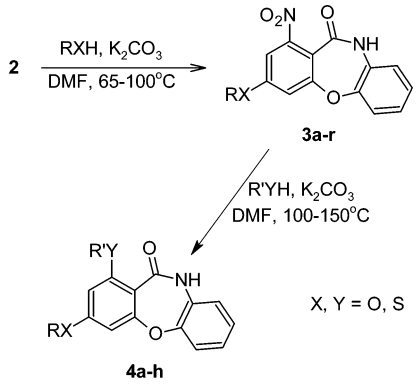

TABLE 1. Reaction Conditions and Yields of 1-Nitro-3-RX-dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 3a−r

product	RX	*T*, h	*T*, °C	yield, %
3a	MeO	15 (1[a])	65 (100[a])	84 (81[a])
3b	EtO	20	75	75
3c	PrO	24	90	19
3d	*i*-PrO	30	80	no reaction
3e	*cyclo*-$C_6H_{11}O$	30	80	no reaction
3f	HOC_2H_4O	10	100	87
3g	$C_6H_5CH_2O$	60	80	63
3h	PhO	3	80	88
3i	3-MeC_6H_4O	3	80	94
3j	4-MeC_6H_4O	3	80	96
3k	2-$MeOC_6H_4O$	3	80	94 (96[b])
3l	4-$MeOC_6H_4O$	3	80	100
3m	2-BrC_6H_4O	3	80	71
3n	4-BrC_6H_4O	3	80	96
3o	$PhCH_2S$	3	80	90
3p	BuS	3	80	93
3q	PhS	3	70	74
3r	4-$CH_3C_6H_4S$	3	70	60

[a] Using NaOMe instead of MeOH and K_2CO_3. [b] With 2 equiv of guaiacol.

TABLE 2. Reaction Conditions and Yields of 1-R′Y-3-RX-Dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 4a−h

product	starting compd	R′Y	RX	*t* h	*T* °C	yield %
4a	**2**	PhO	PhO	8	150	67
4b	**2**	3-$CH_3C_6H_4O$	3-$CH_3C_6H_4O$	8	150	48
4c	**3p**	PhO	BuS	8	150	55
4d	**3a**	BuS	MeO	5	100	31
4e	**3a**	$PhCH_2S$	MeO	5	100	34
4f	**3h**	4-$CH_3C_6H_4S$	PhO	5	120	52
4g	**2**	4-$CH_3C_6H_4S$	4-$CH_3C_6H_4S$	5	120	58
4h	**2**	BuS	BuS	5	100	49

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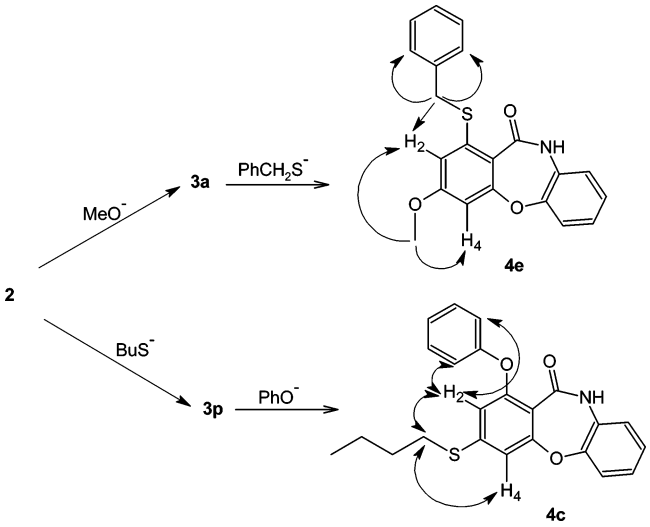
SCHEME 4



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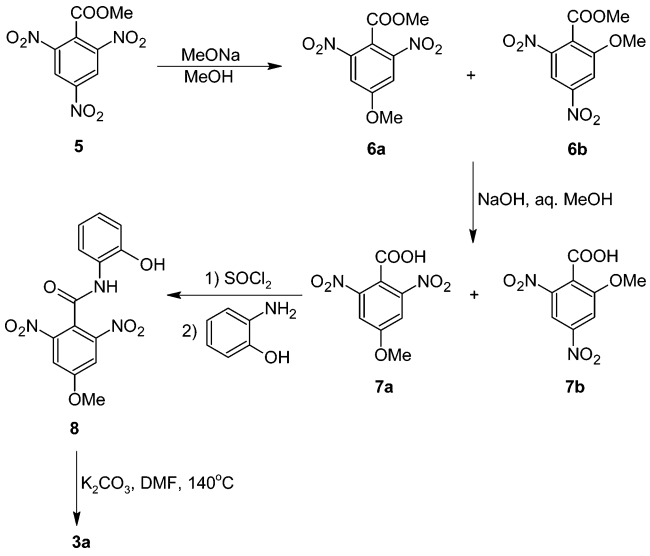

signals of *ortho*-phenyl (δ 6.92) protons and H(2) (δ 6.60) was observed. These facts suggest that the BuS substituent is located in position 3, and the PhO group occupies position 1.

On the basis of this evidence, we concluded that the 3-NO_2 group (remote from the ring fusion point) was substituted first upon the attack of **2** with both O-nucleophiles (MeO^-, preparation of **4e**) and S-nucleophiles (BuS^-, preparation of **4c**). We further confirmed the regiochemistry of substitution by an alternative synthetic approach to **3a** (Scheme 5).

Nucleophilic displacement of the nitro group in methyl 2,4,6-trinitrobenzoate **5** with methoxide anion proceeded with low selectivity to yield a mixture of regioisomeric esters **6a** and **6b**. The ratio of para- to ortho-substitution product was 63:37 (lit.[14] data 5:4). The mixture was further subjected to an alkaline hydrolysis, and the resulting regioisomeric acids **7a** and **7b** were easily separated due to their different solubility in the media. 2,6-Dinitro-4-methoxybenzoic acid **7a** was converted to

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SCHEME 6

o-hydroxyanilide **8**. The intramolecular cyclization of the latter with K_2CO_3 in DMF afforded compound **3a**, which was identical to the product prepared from 1,3-dinitrodibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one **2** via displacement of the nitro group with methoxide anion.

Notably, this selectivity of nucleophilic substitution was unexpected. To the best of our knowledge, a nucleophilic displacement of a *peri*-nitro group (that is, the one adjacent to ring fusion point) in related heterocyclic systems including phthalimides,[15] benzo[*b*]thiophenes,[16] benz[*d*]isoxazoles,[17] and indazoles[18] occurred first[19] (Scheme 6).

In general, for both 1-X-2,4-dinitro- and 1-X-2,4,6-trinitrobenzenes nitro groups in ortho-position to the substituent X usually are substituted first[20] (a heterocycle annulated to benzene ring could be viewed as a special case of substituent). Nevertheless, bulky substituents (e.g., X = *t*-Bu,[20a] COOMe[14]) could direct the nucleophilic attack into para-position by hindering ortho-regions. Moreover, with tertiary amides of 2,4,6-trinitrobenzoic acid (X = $CONR_2$) ortho-substitution product is not formed at all.[6] Considering this evidence, we speculated that for the seven-membered heterocycle annulated to benzene ring, sterical hindrance for the nucleophilic attack at peri-position could be more significant when compared to a previously studied heterocyclic systems with benzoannulated five-membered heterocycle. This could be due to the different geometry of the molecule. At least semiempirical calculation (method AM1, CS MOPAC application) demonstrated that the distance between *peri*-carbon atom and oxygen atom of the carbonyl group is noticeably shorter in 1,3-dinitrodibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one **2** than that in 3,5-dinitrophthalimide[15b] (2.95 Å versus 3.20 Å, respectively) (Scheme 7).

It must be mentioned, however, that primary and secondary amides of 2,4-dinitro- and 2,4,6-trinitrobenzoic acids (X = $CONH_2$, CONHR) provide for high ortho-selectivity of the nucleophilic substitution.[6,21,22] This fact

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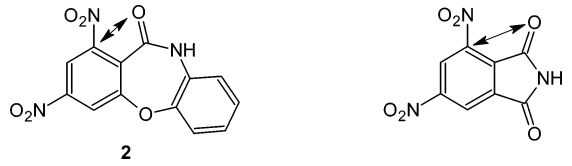
SCHEME 7



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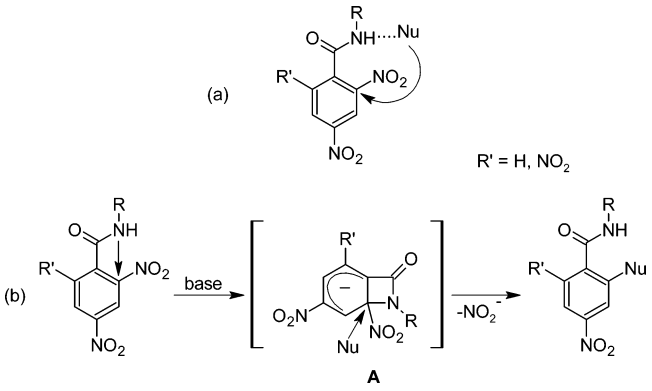

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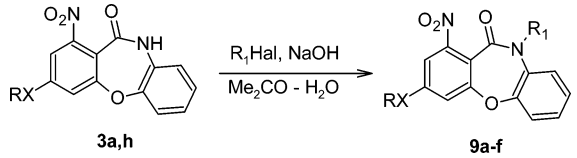

could not be explained by steric or electronic reasons (cf. ortho-/para- ratio of ca. 10:1[6] for X = CONHMe and CONHBu^t and 37:63 for X = COOMe). Involvement of an amide NH in stabilization of a transition state could be an additional powerful factor facilitating ortho-attack[6] (Scheme 8a). Alternatively, participation of the amide nitrogen in intramolecular nucleophilic substitution reaction leading to a benzazetidine intermediate **A** (Scheme 8b) could be envisaged.

The exact mechanism remains to be clarified, but the putative "NH-proton effect" cannot affect the nucleophilic substitution in dibenz[*b*,*f*][1,4]oxazepinone **2** anyway. In this molecule, the amide nitrogen is distanced from the *peri*-carbon atom, as CONH fragment is a part of the seven-membered ring. The reaction regiochemistry is driven by a steric hindrance for peri-attack caused by the carbonyl group.

Interestingly, this change in regioselectivity between benzoannulated five-membered heterocycles and dibenz-[*b*,*f*][1,4]oxazepinone-10(11*H*)-ones is observed not only for the substitution of the nitro group. Thus, a reaction of fluorine displacement for N-substituted 3-fluorophthalimides (F atom in peri-position) proceeds more rapidly than for their 4-fluoro isomers.[15a] In contrast, in 1,2,3,4-tetrafluorodibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one fluorine atom in remote position 3 is displaced first.[23]

Further, dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones **3** underwent N-alkylation with different alkyl halides in the presence of a base (Scheme 9). In particular, with 3-(dimethylamino)propyl chloride as alkylating agent (R_1 = $Me_2N(CH_2)_3$) product **9b** (Sintamil analog[3]) is prepared from **3a**.

Experimental Section

***N*-(2-Hydroxyphenyl)-2,4,6-trinitrobenzamide (1).** In a 10-L flask, to a suspension of 2,4,6-trinitrobenzoyl chloride (485 g, 1.76 mol) in dry benzene (9 L), 2-aminophenol (385 g, 3.53 mol) was added portionwise, and the mixture was refluxed for 8 h. The resulting precipitate was filtered off, washed with benzene (3 × 800 mL) and hot water (15 × 1.5 L), and dried. Yield: 505 g (82%), mp 201−203 °C. ^{1}H NMR (DMSO-d_6, δ): 6.8−7.0 (m, 3H), 8.05 (d, J = 8.3 Hz, 1H), 9.10 (s, 2H), 9.70 (br s, 1H), 10.35 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 348 [M$^+$, 5], 153 [69], 108 [99], 79 [100]. Anal. Calcd for $C_{13}H_8N_4O_8$: C, 44.84; H, 2.32; N, 16.09. Found: C, 45.20; H, 2.15; N, 15.91.

1,3-Dinitrodibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one (2). In a 5-L jar, to a solution of the anilide **1** (505 g, 1.45 mol) in a mixture of MeOH (1.9 L) and MeCN (1.9 L), 25% aqueous NH_3 (400 mL) was added. The lid was tightly closed, and the mixture was heated at 50 °C for 120 h (stirring was not needed). Then the resulting precipitate was filtered off, washed with MeOH (1 L), and dried. Yield: 376 g (86%), black needles. This product was sufficiently pure for synthetic purposes (and pure by NMR). An analytical sample could be prepared by column chromatography on silica gel (eluent benzene/EtOAc 1:1). Orange needles, mp 289−290 °C. ^{1}H NMR (DMSO-d_6, δ): 7.15−7.30 (m, 3H), 7.48 (d, J = 8.2 Hz, 1H), 8.49 (s, 1H), 8.51 (s, 1H), 11.20 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 301 [M$^+$, 49], 211 [32], 126 [94], 74 [100]. Anal. Calcd for $C_{13}H_7N_3O_6$: C, 51.84; H, 2.34; N, 13.95. Found: C, 52.15; H, 2.52; N, 13.60.

Preparation of 1-Nitro-3-RX-dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 3a−r (General Procedure). To prepare compounds **3h**−**r**, to a suspension of 1,3-dinitrodibenz[*b*,*f*][1,4]-oxazepine-11(10*H*)-one **2** (1.50 g, 5 mmol) and anhydrous K_2CO_3 (0.76 g, 5.5 mmol) in DMF (20 mL), a corresponding reagent RXH (5.5 mmol) was added upon stirring. Temperatures and reaction times are given in Table 1. Upon cooling, the reaction mixture was poured in water (200 mL) and neutralized with HCl. The precipitate was filtered off, successively washed with hot water (20 mL) and MeOH (5 mL), and dried. Compound **3q** was additionally crystallized from benzene, while **3r** was washed with hot benzene to remove disulfides formed as side products.

In reaction with alcohols (preparation of compounds **3a**−**g**), 50 mmol of the corresponding alcohol and 12 mmol of K_2CO_3 were used for 5 mmol of **2**.

Product **3a** was also prepared according to the above procedure for **3h**−**r** using MeONa instead of MeOH and K_2CO_3.

3-Methoxy-1-nitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (3a): mp 268−270 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 3.90 (s, 3H), 7.15−7.25 (m, 4H), 7.28 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 10.65 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 286 [M$^+$, 100], 241 [35]. Anal. Calcd for $C_{14}H_{10}N_2O_5$: C, 58.74; H, 3.52; N, 9.79. Found: C, 58.60; H, 3.64; N, 9.69.

1-Nitro-3-phenoxydibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one (3h): mp 223−224 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 7.13 (s, 1H), 7.15 (d, J = 8.1 Hz, 1H), 7.20−7.28 (m, 5H), 7.30 (t, J = 8.1 Hz, 2H), 7.48−7.53 (m, 2H), 10.77 (br s, NH). EI-MS (70 eV) (*m*/*z*, *I*, %): 348 [M$^+$, 80], 303 [43], 211 [12], 77 [100]. Anal. Calcd for $C_{19}H_{12}N_2O_5$: C, 65.52; H, 3.47; N, 8.04. Found: C, 65.40; H, 3.56; N, 7.98.

3-Butylsulfanyl-1-nitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (3p): mp 199−202 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 0.90 (t, J = 7.2 Hz, 3H), 1.44 (m, 2H), 1.63 (m, 2H), 3.15 (t, J = 7.1 Hz, 2H), 7.2−7.3 (m, 3H), 7.41 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 2.1 Hz, 1H), 7.63 (d, J = 2.1 Hz, 1H), 10.80 (br s, 1H).

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Anal. Calcd for $C_{17}H_{16}N_2O_4S$: C, 59.29; H, 4.68; N, 8.13; S, 9.31. Found: C, 59.55; H, 4.80; N, 7.95; S, 9.49.

1-Nitro-3-phenylsulfanyldibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (3q): mp 240−241 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 7.08 (t, J = 7.8 Hz, 1H), 7.14−7.20 (m, 4H), 7.23 (d, J = 7.9 Hz, 1H), 7.52 (m, 3H), 7.57 (m, 2H), 10.71 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 364 [M$^+$, 100], 319 [47]. Anal. Calcd for $C_{19}H_{12}N_2O_4S$: C, 62.63; H, 3.32; N, 7.69; S, 8.80. Found: C, 62.57; H, 3.38; N, 7.60; S, 8.85.

3-(4-Methylphenyl)sulfanyl-1-nitrodibenz[*b*,*f*][1,4]-oxazepin-11(10*H*)-one (3r): mp 269−270 °C (MeCN) (dec). ^{1}H NMR (DMSO-d_6, δ): 2.44 (s, 3H), 7.07−7.24 (m, 6H), 7.34 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 10.71 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 378 [M$^+$, 100], 333 [52], 123 [51]. Anal. Calcd for $C_{20}H_{14}N_2O_4S$: C, 63.48; H, 3.73; N, 7.40; S, 8.47. Found: C, 63.22; H, 3.81; N, 7.50; S, 8.39.

Preparation of 1-R′Y-3-RX-dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 4a−h (General Procedure). To prepare compounds **4c**−**f**, to a suspension of the corresponding compound **3** (5 mmol) and anhydrous K_2CO_3 (0.76 g, 5.5 mmol) in DMF (20 mL), a corresponding reagent R′YH (5.5 mmol) was added upon stirring. Temperatures and reaction times are given in Table 2. Upon cooling, the reaction mixture was poured in water (200 mL) and neutralized with HCl. The precipitate was filtered off, successively washed with hot water (20 mL) and MeOH (5 mL), and crystallized from benzene.

To prepare the products **4a**,**b**,**g**,**h**, dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-one **2** (1.50 g, 5 mmol) was used as a starting compound, and 11 mmol of both K_2CO_3 and corresponding reagent was taken.

1,3-Diphenoxydibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (4a): mp 227−230 °C. ^{1}H NMR (DMSO-d_6, δ): 6.28 (s, 1H), 6.69 (s, 1H), 6.94 (d, J = 8.1 Hz, 2H), 7.10 (m, 5H), 7.20 (m, 2H), 7.32 (m, 3H), 7.40 (t, J = 8.1 Hz, 2H), 10.25 (br s, 1H). Anal. Calcd for $C_{25}H_{17}NO_4$: C, 75.94; H, 4.33; N, 3.54. Found: C, 75.77; H, 4.39; N, 3.67.

3-Butylsulfanyl-1-phenoxydibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (4c): mp 128−129 °C. ^{1}H NMR (DMSO-d_6, δ): 0.82 (t, J = 7.2 Hz, 3H), 1.33 (m, 2H), 1.52 (m, 2H), 2.94 (t, J = 7.1 Hz, 2H, SCH_2), 6.60 (s, 1H, H(2)), 6.92 (d, J = 8.1 Hz, 2H, *o*-Ph), 7.08 (s, 1H, H(4)), 7.13 (m, 3H), 7.20 (t, J = 8.1 Hz, 1H), 7.35 (m, 3H), 10.31 (br s, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 391 [M$^+$, 92], 335 [100], 302 [48]. Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58; S, 8.19. Found: C, 70.82; H, 5.54; N, 3.33; S, 8.06.

1-Benzylsulfanyl-3-methoxydibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (4e): mp 179−181 °C.^{1}H NMR (DMSO-d_6, δ): 3.80 (s, 3H, OCH_3), 4.18 (s, 2H, SCH_2), 6.72 (d, J = 1.9 Hz, 1H, H(2)), 6.82 (d, J = 1.9 Hz, 1H, H(4)), 7.11 (m, 2H), 7.17 (t, J = 8.0 Hz, 1H), 7.23 (t, J = 8.1 Hz, 1H), 7.30 (m, 3H), 7.38 (d, J = 8.0 Hz, 1H), 10.31 (br s, 1H). Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71; N, 3.85; S, 8.82. Found: C, 69.52; H, 4.79; N, 3.58; S, 8.99.

4-Methoxy-2,6-dinitrobenzoic Acid (7a) and 2-Methoxy-4,6-dinitrobenzoic Acid (7b). To a suspension of methyl 2,4,6-trinitrobenzoate **5**[24] (80.0 g, 0.295 mmol) in MeOH (460 mL), a solution of NaOMe (16.8 g, 0.311 mol) in MeOH (150 mL) was added. The mixture was refluxed for 40 min, then MeOH was evaporated to $^1/_{10}$ of the initial volume, and the precipitate was filtered off and washed with water (3 × 200 mL). The product is a mixture of methyl 4-methoxy-2,6-dinitro- and methyl 2-methoxy-4,6-dinitrobenzoates in 63:37 ratio (according to NMR data). Yield: 65.0 g (86%).

To a solution of NaOH (11.4 g, 0.285 mol) in water (500 mL) and MeOH (50 mL), the mixture of methyl 4-methoxy-2,6-dinitro- and methyl 2-methoxy-4,6-dinitrobenzoates (65.0 g, 0.254 mol) was added. The reaction mixture was stirred at 80 °C for ca. 3 h (the reaction progress was monitored by TLC; eluent EtOAc/heptane 1:3). The hot clear solution was acidified until it became turbid and then cooled to room temperature, and the precipitate of 4-methoxy-2,6-dinitrobenzoic acid **7a** was filtered off. Yield: 31.3 g (47% with respect to methyl 2,4,6-trinitrobenzoate **5**). mp 181 °C (lit.[14] mp 179−180 °C). ^{1}H NMR (DMSO-d_6, δ): 3.99 (s, 3H), 7.98 (s, 2H); 14.0−14.5 (br s, 1H).

The mother liquor remaining after precipitation of **7a** was evaporated to dryness, and the residue was extracted with hot benzene (3 × 500 mL). The combined extracts were cooled to room temperature, and the precipitated 2-methoxy-4,6-dinitrobenzoic acid **7b** was filtered off. Yield: 24.0 g (36% with respect to **5**).[25] mp 150−152 °C (lit.[14] mp 150−151 °C). ^{1}H NMR (DMSO-d_6, δ): 4.02 (s, 3H), 8.24 (d, J = 2.0 Hz, 1H), 8.43 (d, J = 2.0 Hz, 1H), 14.0−14.5 (br s, 1H).

***N*-(2-Hydroxyphenyl)-2,6-dinitro-4-methoxybenzamide (8).** A suspension of 2,6-dinitro-4-methoxybenzoic acid **7a** in $SOCl_2$ (5-fold molar excess) was refluxed for 30 min (until the gas evolution ceased), and excess $SOCl_2$ was removed in vacuo. The resulting oil soon solidified. 2,6-Dinitro-4-methoxybenzoyl chloride thus obtained (mp 100−101 °C after crystallization from benzene) was converted to anilide **8** under the action of 2-aminophenol as described for the compound **1**. Yield: 72%, mp 232−234 °C. ^{1}H NMR (DMSO-d_6, δ): 4.00 (s, 3H), 6.82 (t, J = 8.1 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.98 (t, J = 8.2 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 8.00 (s, 2H), 9.63 (br s, 1H), 10.12 (br s, 1H). Anal. Calcd for $C_{14}H_{11}N_3O_7$: C, 50.46; H, 3.33; N, 12.61. Found: C, 50.58; H, 3.22; N, 13.00.

Cyclization of *N*-(2-Hydroxyphenyl)-2,6-dinitro-4-methoxybenzamide 8 (Alternative Synthesis of 3a). A suspension of the anilide **8** (1.67 g, 5 mmol) and anhydrous K_2CO_3 (0.76 g, 5.5 mmol) in DMF (20 mL) was stirred at 120 °C for 3 h, whereupon the reaction mixture was worked up as described above in the general procedure for compounds **3a**−**r**. Yield of **3a** was 68%.

Preparation of Dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 9a−f by N-Alkylation of 3a,h (General Procedure). To a stirred suspension of dibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one **3a** (**3h**) (3 mmol) in acetone (10 mL), 2.5 M aqueous solution of NaOH (1.3 mL) was added, the temperature was raised to ~60 °C, and the corresponding alkyl halide (5 mmol) was introduced. The reaction mixture was refluxed with stirring for 2 h, then additional portions of 2.5 M aqueous NaOH (0.6 mL) and alkyl halide (2 mmol) were added. In 2 h the addition of aqueous alkali and alkyl halide was repeated again, and stirring was continued for 5 h more. Then acetone was removed from the reaction mixture in vacuo, the residue was extracted with ether (3 × 10 mL), and the combined extracts were dried with $MgSO_4$ and evaporated to dryness. The residue was crystallized from *i*-PrOH. Yields of the products **9a**−**f** are given in Table 3.

TABLE 3. Yields of Dibenz[*b*,*f*][1,4]oxazepine-11(10*H*)-ones 9a−f (N-Alkylation of Compounds 3a,h)

product	starting compd	RX	R_1	yield, %
9a	**3a**	MeO	Bu	51
9b	**3a**	MeO	$Me_2N(CH_2)_3$	32[a]
9c	**3h**	PhO	Me	56
9d	**3h**	PhO	CH_2=$CHCH_2$	58
9e	**3h**	PhO	4-$O_2NC_6H_4CH_2$	43
9f	**3h**	PhO	$PhCOCH_2$	48

[a] Isolated as a hydrochloride.

10-Butyl-3-methoxy-1-nitrodibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-one (9a). BuBr is used as alkylating agent. mp 132−133 °C. ^{1}H NMR (DMSO-d_6, δ): 0.91 (t, J = 7.5 Hz, 3H), 1.36 (m, 2H), 1.62 (t, J = 7.5 Hz, 2H), 3.6−4.4 (br s, 2H), 3.91 (s, 3H), 7.09 (br s, 1H), 7.21 (m, 2H), 7.31 (m, 2H), 7.52 (d, J = 8.0 Hz, 1H). EI-MS (70 eV) (*m*/*z*, *I*, %): 342 [M$^+$, 81], 286 [99], 182 [82], 106 [100]. Anal. Calcd for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 62.89; H, 5.21; N, 8.44.

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(25) Earlier (see ref 14), 2-methoxy-4,6-dinitrobenzoic acid was prepared in 5% yield from 2-methoxy-4,6-dinitrotoluene. The procedure described here is by far preferable.

10-(3-(Dimethylamino)propyl)-3-methoxy-1-nitrodibenz-[*b*,*f*][1,4]oxazepin-11(10*H*)-one Hydrochloride (9b). 3-(Dimethylamino)propyl chloride hydrochloride was used as alkylating agent. To the dried ethereal extract, concentrated HCl (0.5 mL) was added with stirring, and the resulting precipitate was filtered off and washed with ether. mp 242−245 °C. ^{1}H NMR (DMSO-d_6, δ): 2.02 (m, 2H), 2.70 (s, 6H), 3.06 (m, 2H), 3.90 (s, 3H), 4.1 (br s, 2H), 7.3−7.4 (m, 4H), 7.47 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 10.35 (br s, 1H). Anal. Calcd for $C_{19}H_{21}N_3O_5$·HCl: C, 55.95; H, 5.44; Cl, 8.69; N, 10.30. Found: C, 55.82; H, 5.48; Cl, 8.65; N, 10.37.

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Supporting Information Available: Characterization data for compounds **3b**,**c**,**f**,**g**,**i**−**o**, **4b**,**d**,**f**−**h**, and **9c**−**f**, ^{1}H NMR spectrum for **7b**, and NOE measurements for **4c**,**e** (2D NOESY spectrum for **4c** and NOE difference spectrum for **4e**). This material is available free of charge via the Internet at http://pubs.acs.org.

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