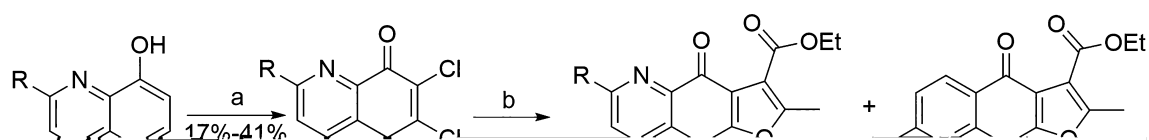
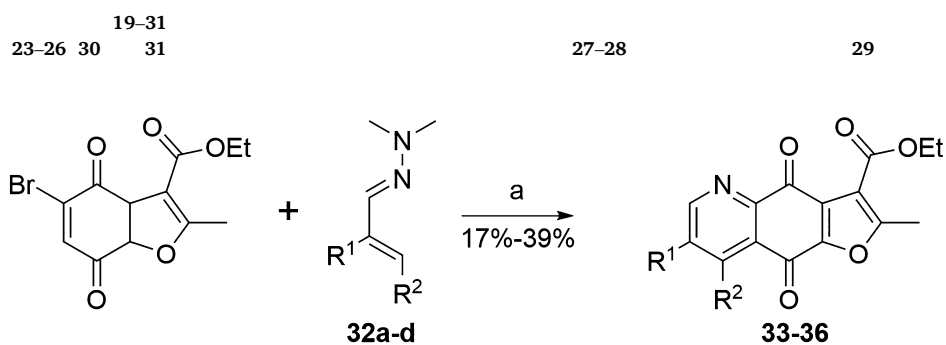




$$2 = \mu_5 \text{ ud.n} \quad \text{n} \quad \text{On}$$

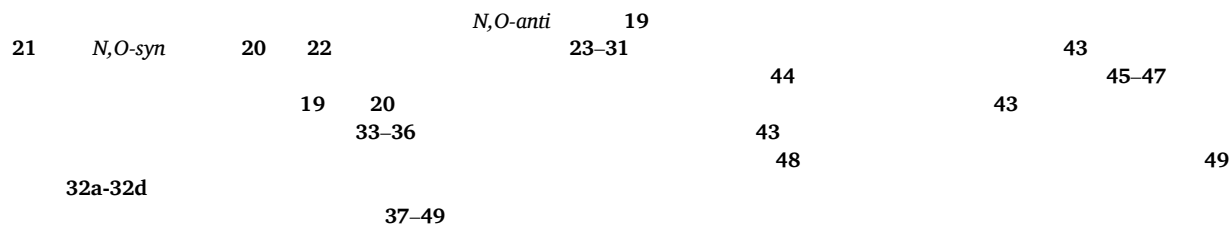


Scheme 2.



Scheme 3.

33-36

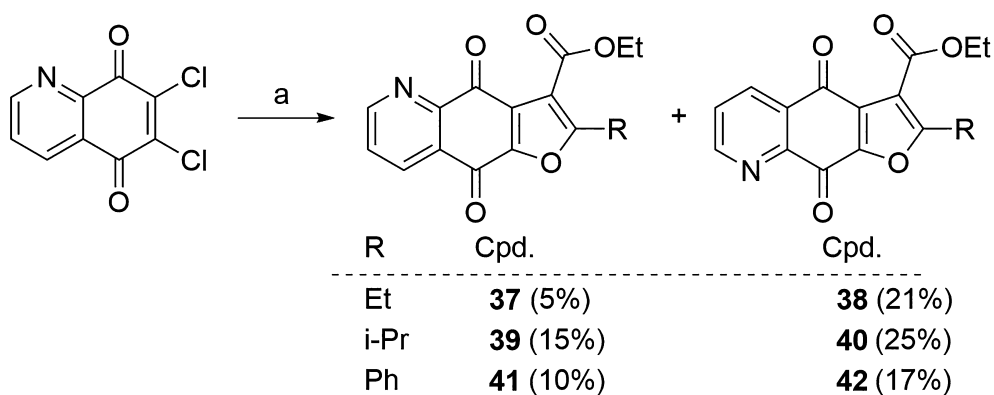


32a-32d

*N,O-anti**N,O-syn*

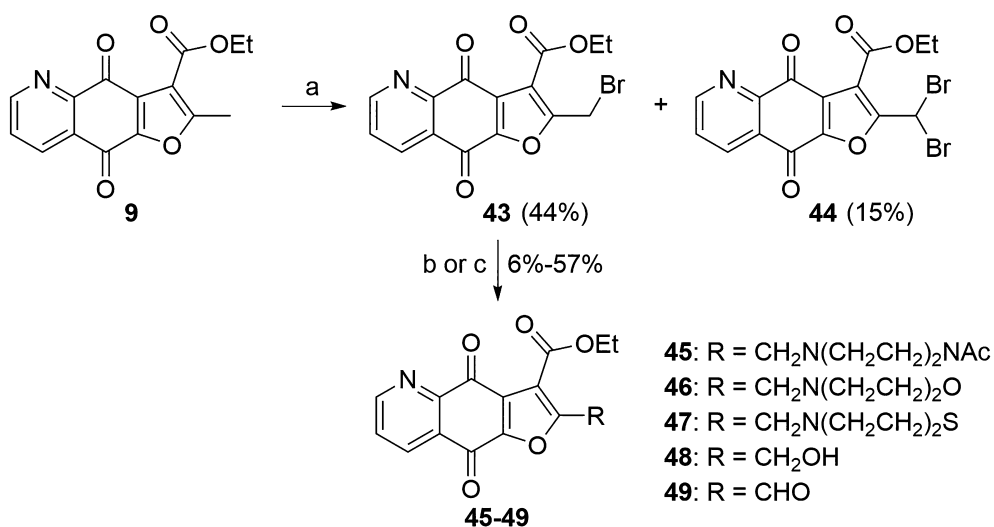
9

52



Scheme 4.

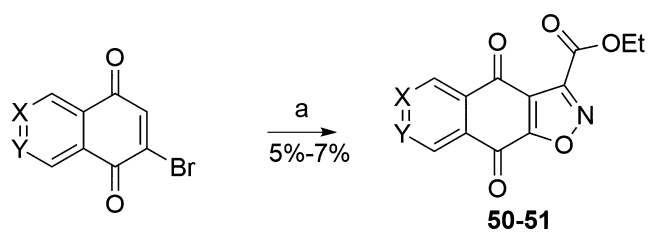
37–42



Scheme 5.

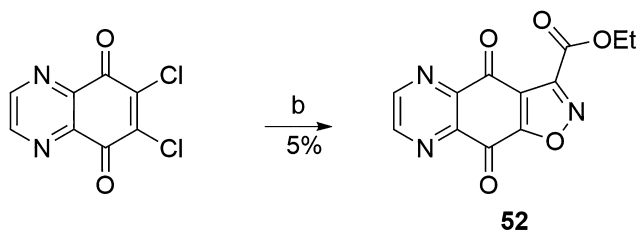
48	49	43–49	45–47
Z			N,O-anti
54–57	53		N,O- N,O-
50	51 58a–e	59–63 64a–g	37 ± μ 38 > μ 39 ±
65–71			40 > μ 41 ± μ 42 ± μ
			11 > μ 14 > μ
			12 ± μ 13 > μ
			16 > μ
			9 ± μ
			25–29 > μ 24 ± μ 36
			30–33 ± μ 35 ± μ 34 > μ
			9 49 ± μ
			37 39 41 45–47

## 2.2. Enzyme inhibition assays

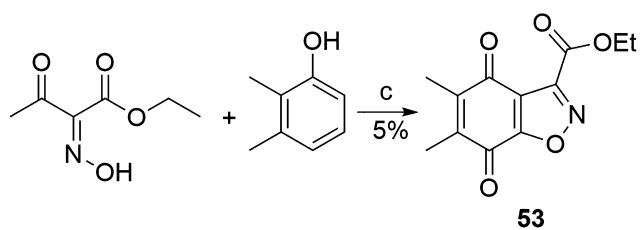


**50:** X = N, Y = CH

**51:** X = CH, Y = N



### 2.3. Molecular modeling



Scheme 6.

50-53

70

48 >  $\mu$

B

$\pi \pi$

$\mu$  **50**  $\pm$   $\mu$  **51**  $\pm$   $\mu$  **10**  $\pm$   
**53** >  $\mu$

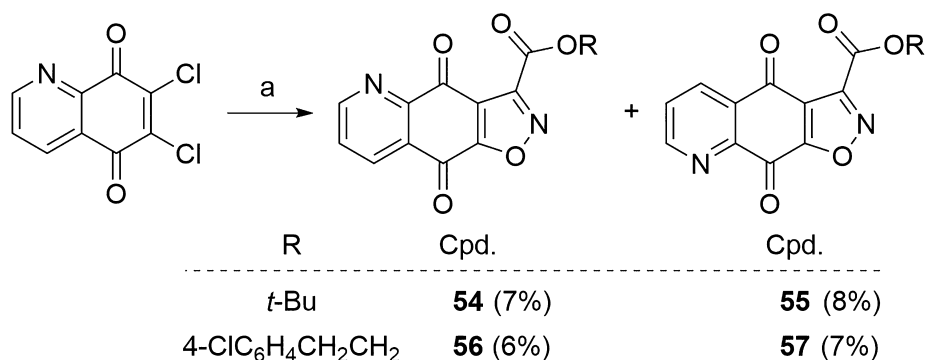
**54-57** **59-63**

$\pm$   $\pm$   $\mu$

### 3. Conclusions

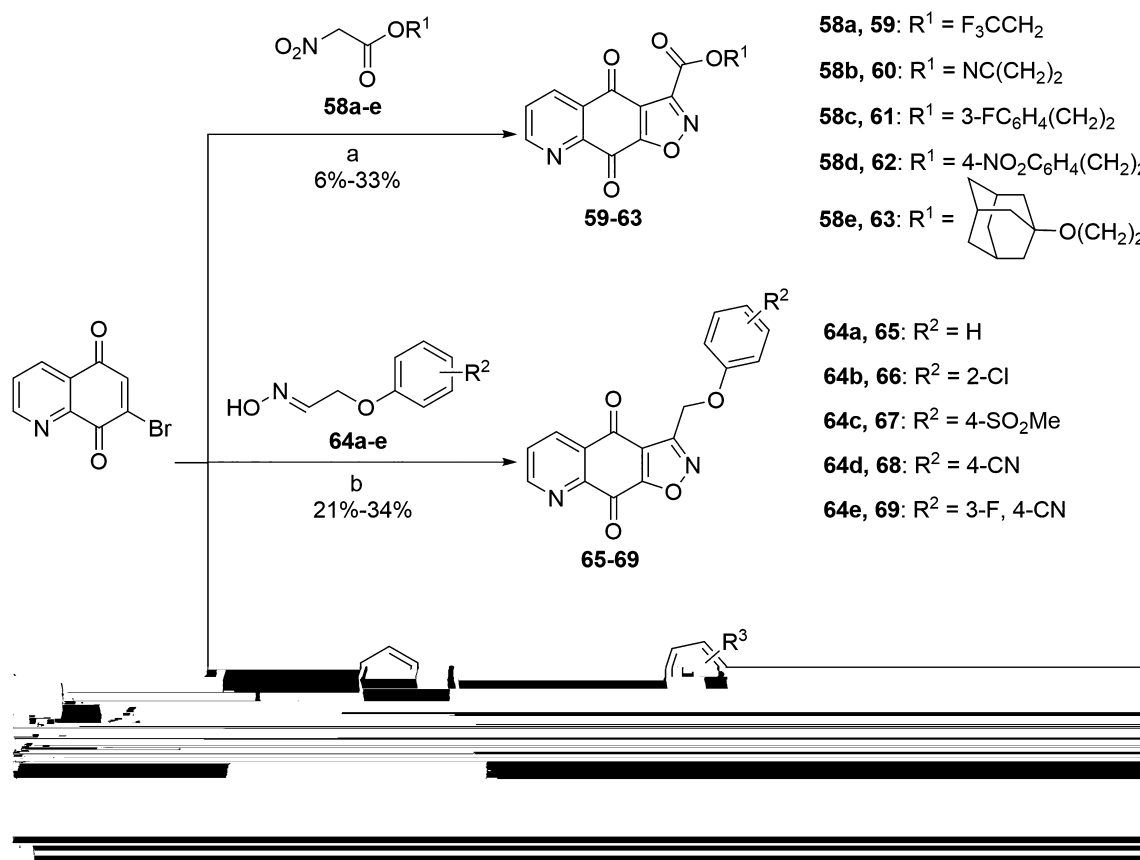
**65-71**

**65-71**



Scheme 7.

54-57.



Scheme 8.

59–63 65–71

Table 1

$\mu$		$\mu$		$\mu$	
1	$\pm$	31	>	51	$\pm$
11	>	33	>	52	$\pm$
12	$\pm$	34	>	53	>
13	>	35	$\pm$	54	$\pm$
14	$\pm$	36	$\pm$	55	$\pm$
15	>	37	$\pm$	56	$\pm$
16	>	38	>	57	$\pm$
19	$\pm$	39	$\pm$	59	$\pm$
20	>	40	>	60	$\pm$
21	$\pm$	41	$\pm$	61	$\pm$
22	>	42	$\pm$	62	$\pm$
23	$\pm$	43	$\pm$	63	$\pm$
24	$\pm$	44	$\pm$	65	$\pm$
25	>	45	$\pm$	66	$\pm$
26	>	46	$\pm$	67	$\pm$
27	>	47	$\pm$	68	$\pm$
28	>	48	>	69	$\pm$
29	>	49	$\pm$	70	$\pm$
30	>	50	$\pm$	71	$\pm$

 $\pm$ 

## 4. Methods and materials

## 4.1. General experiments

 $\mu$ 

49

 $\pm$  $\mu$ 

&gt;

 $\mu$  $\mu$

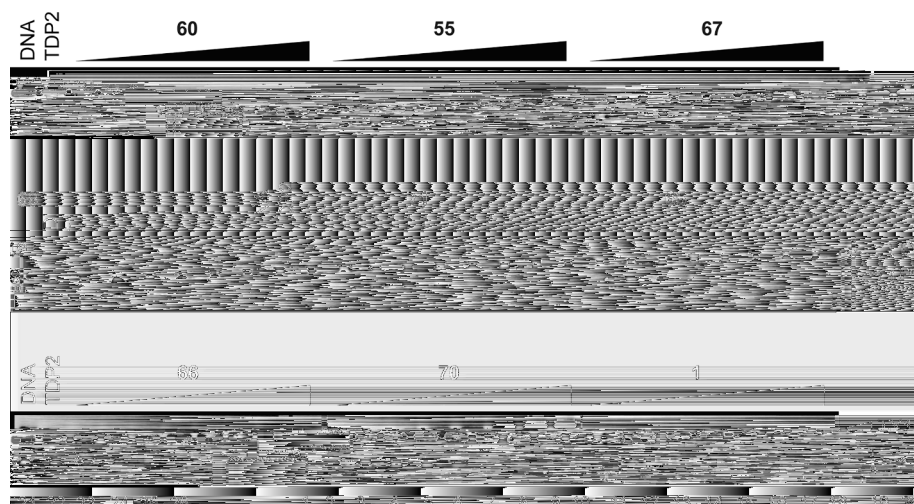


Fig. 2.

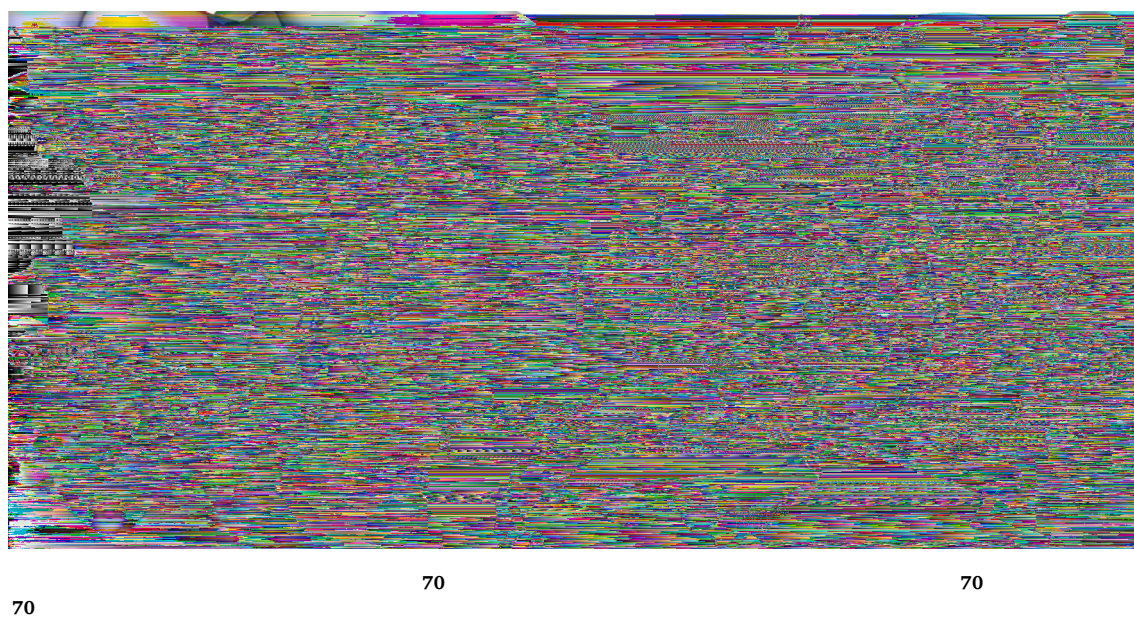
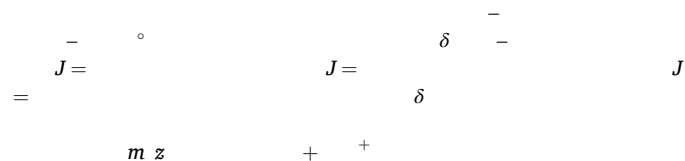


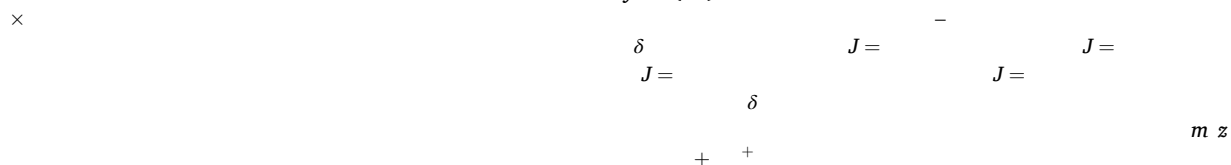
Fig. 3.

#### 4.2. General procedure for the synthesis of compounds 11–14, 16, 19–22, 37–42, 52 and 54–57.

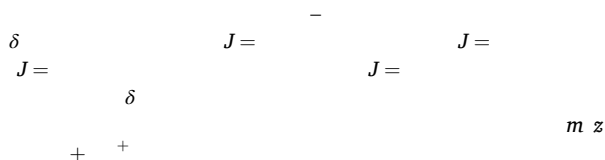
##### 4.2.1. Ethyl 2-methyl-4,9-dioxo-4,9-dihydronaphtho[2,3-b]furan-3-carboxylate (11)



##### 4.2.2. Ethyl 2-methyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]isoquinoline-3-carboxylate (12)



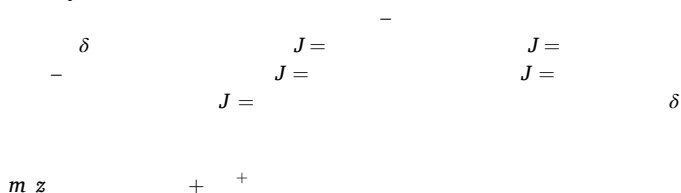
4.2.3. Ethyl 2-methyl-4,9-dioxo-4,9-dihydrofuro[3,2-g]isoquinoline-3-carboxylate (13)



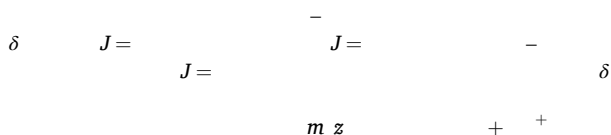
4.2.4. Ethyl 7-methyl-5,9-dioxo-5,9-dihydrofuro[2,3-g]quinoxaline-8-carboxylate (14)



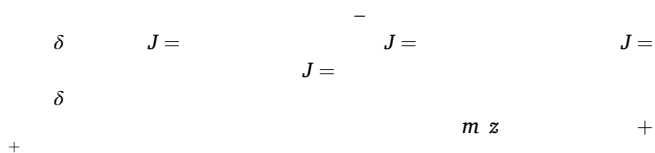
4.2.5. Ethyl 2-methyl-4,11-dioxo-4,11-dihydrofuro[2,3-b]acridine-3-carboxylate (16)



4.2.6. Ethyl-6-chloro-2-methyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (19)



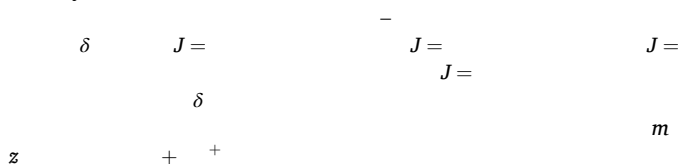
4.2.7. Ethyl-7-chloro-2-methyl-4,9-dioxo-4,9-dihydrofuro[3,2-g]quinoline-3-carboxylate (20)



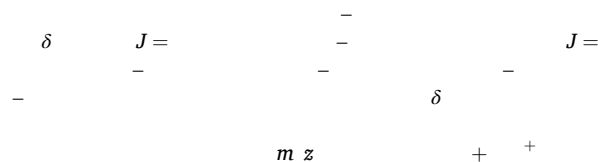
4.2.8. Ethyl-2,6-dimethyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (21)



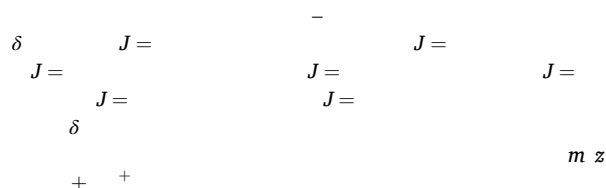
4.2.9. Ethyl-2,7-dimethyl-4,9-dioxo-4,9-dihydrofuro[3,2-g]quinoline-3-Carboxylate (22)



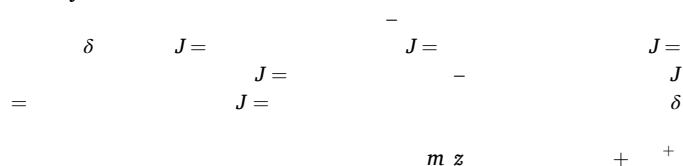
4.2.10. Ethyl 2-isopropyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (37)



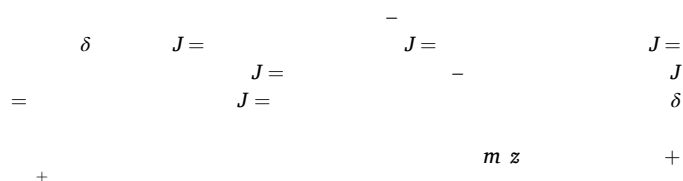
4.2.11. Ethyl 2-isopropyl-4,9-dioxo-4,9-dihydrofuro[3,2-g]quinoline-3-carboxylate (38)



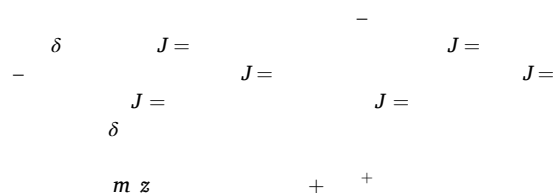
4.2.12. Ethyl 2-isopropyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (39)



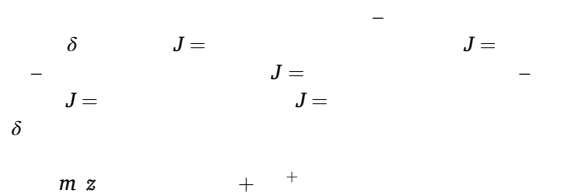
4.2.13. Ethyl 2-isopropyl-4,9-dioxo-4,9-dihydrofuro[3,2-g]quinoline-3-carboxylate (40)



4.2.14. Ethyl 4,9-dioxo-2-phenyl-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (41)



4.2.15. Ethyl 4,9-dioxo-2-phenyl-4,9-dihydrofuro[3,2-g]quinoline-3-carboxylate (42)



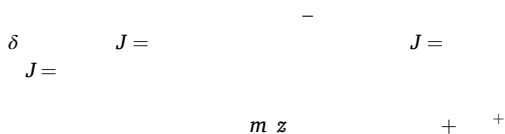
4.2.16. Ethyl-4,9-dioxo-4,9-dihydroisoxazolo[4,5-g]quinoxaline-3-carboxylate (52)



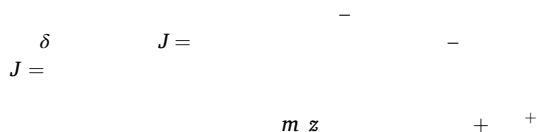


$m/z$  + +

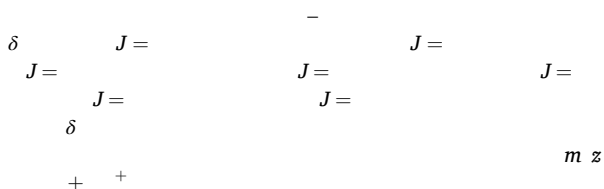
4.2.17. *Tert*-butyl 4,9-dioxo-4,9-dihydroisoxazolo[5,4-*g*]quinoline-3-carboxylate (**54**)



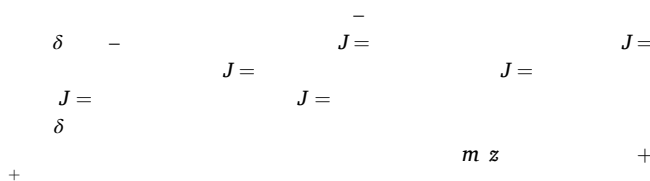
4.2.18. *Tert*-butyl 4,9-dioxo-4,9-dihydroisoxazolo[4,5-*g*]quinoline-3-carboxylate (**55**)



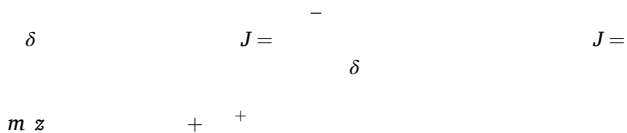
4.2.19. 4-chlorophenethyl 4,9-dioxo-4,9-dihydroisoxazolo[5,4-*g*]quinoline-3-carboxylate (**56**)



4.2.20. 4-chlorophenethyl 4,9-dioxo-4,9-dihydroisoxazolo[4,5-*g*]quinoline-3-carboxylate (**57**)



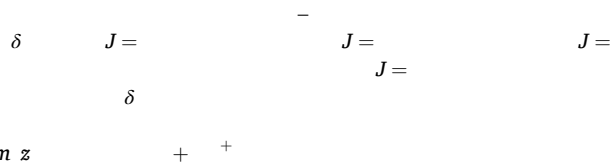
4.3. The synthesis of product **15**.



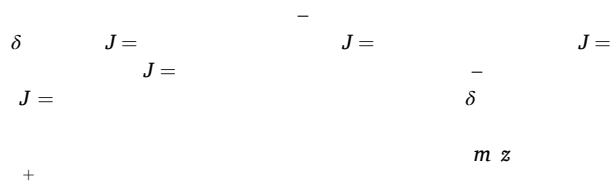
4.4. General procedure for the synthesis of compounds **23–26**, **30** and **31**.

19 20

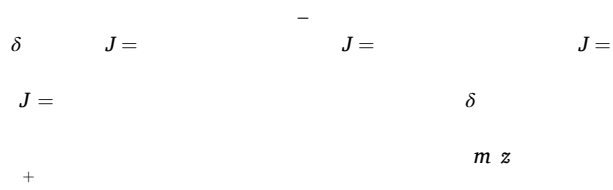
4.4.1. Ethyl-6-(dimethylamino)-2-methyl-4,9-dioxo-4,9-dihydrofuro[2,3-*g*]quinoline-3-carboxylate (**23**).



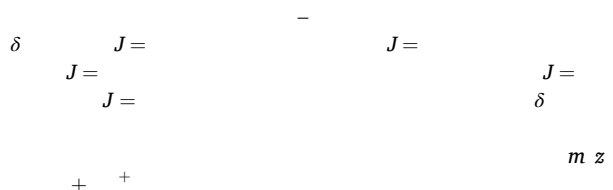
4.4.2. Ethyl-2-methyl-4,9-dioxo-6-(piperidin-1-yl)-4,9-dihydrofuro[2,3-*g*]quinoline-3-carboxylate (**24**)



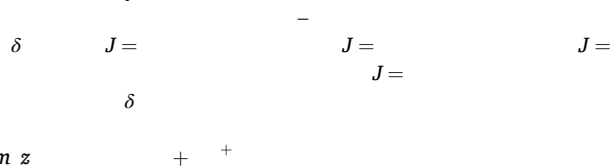
4.4.3. Ethyl-2-methyl-6-(4-methylpiperazin-1-yl)-4,9-dioxo-4,9-dihydrofuro[2,3-*g*]quinoline-3-carboxylate (**25**)



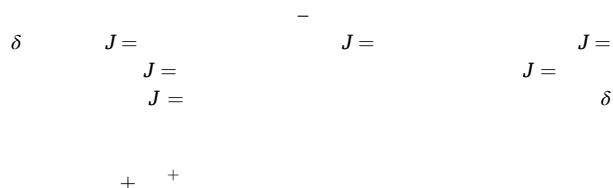
4.4.4. Ethyl-2-methyl-6-(methyl(prop-2-yn-1-yl)amino)-4,9-dioxo-4,9-dihydrofuro[2,3-*g*]quinoline-3-carboxylate (**26**)



4.4.5. Ethyl-7-(dimethylamino)-2-methyl-4,9-dioxo-4,9-dihydrofuro[3,2-*g*]quinoline-3-carboxylate (**30**)



4.4.6. Ethyl-2-methyl-4,9-dioxo-7-(piperidin-1-yl)-4,9-dihydrofuro[3,2-*g*]quinoline-3-carboxylate (**31**)



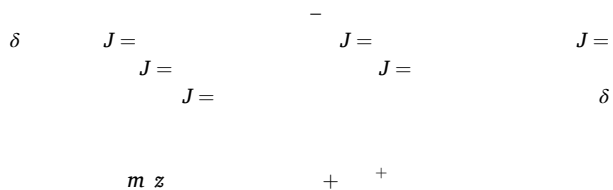
4.5. The synthesis of compounds **27** and **28**.

19 =

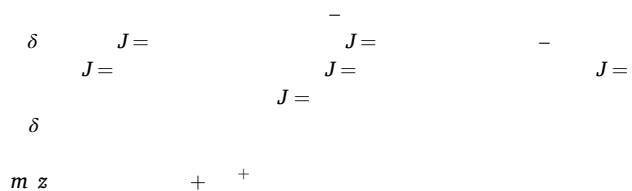
×

27 28

4.5.1. Ethyl-6-(4-methoxyphenyl)-2-methyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (27)

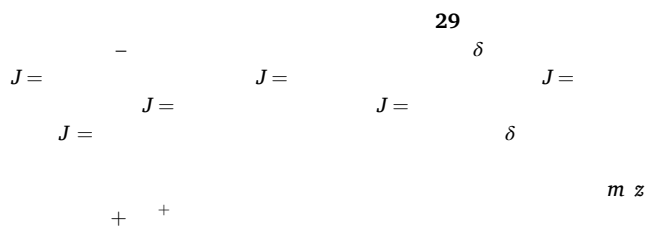


4.5.2. Ethyl-6-(furan-2-yl)-2-methyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (28)



4.6. The synthesis of compound 29.

19

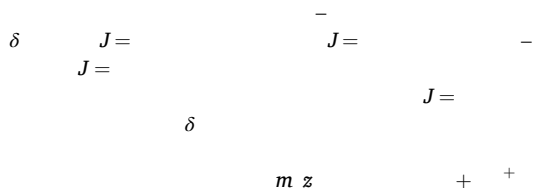


4.7. General procedure for the synthesis of compounds 33–36.

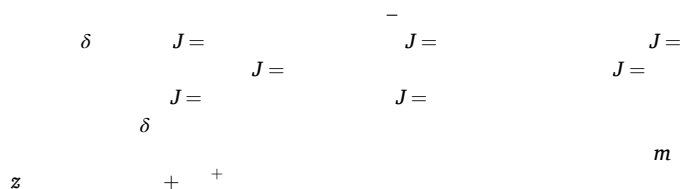
32a-d

×

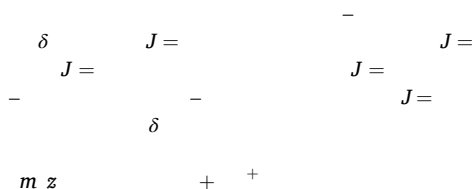
4.9.1. Ethyl 2-((4-acetylpiperazin-1-yl)methyl)-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (**45**)



4.9.2. Ethyl 2-(morpholinomethyl)-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (**46**)



4.9.3. Ethyl 4,9-dioxo-2-(thiomorpholinomethyl)-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (**47**)



4.10. The synthesis of compounds **48** and **49**

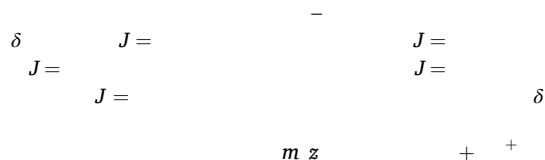
**43**

**43**

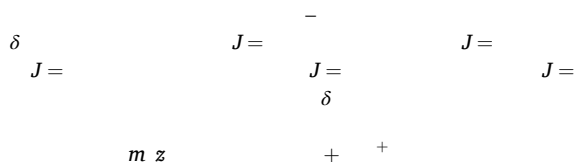
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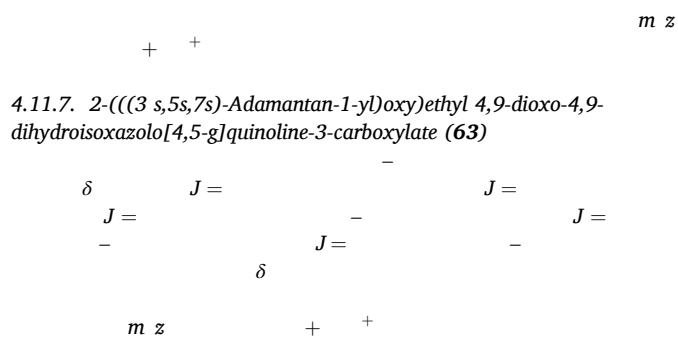
**48**    **49**

4.10.1. Ethyl-2-(hydroxymethyl)-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (**48**)

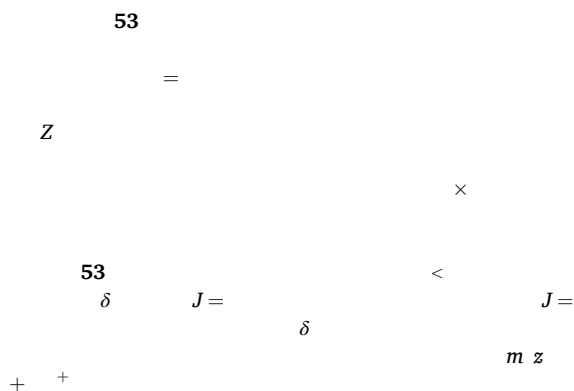


4.10.2. Ethyl-2-formyl-4,9-dioxo-4,9-dihydrofuro[2,3-g]quinoline-3-carboxylate (**49**)





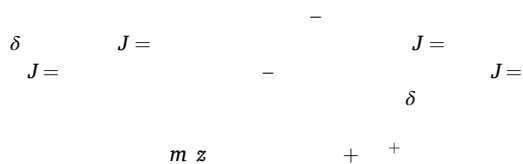
4.12. The synthesis of **53**.



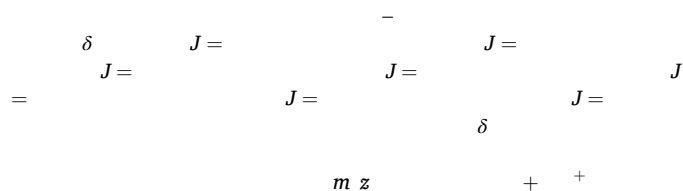
4.13. General procedure for the synthesis of compounds **65–71**.

**65–71**

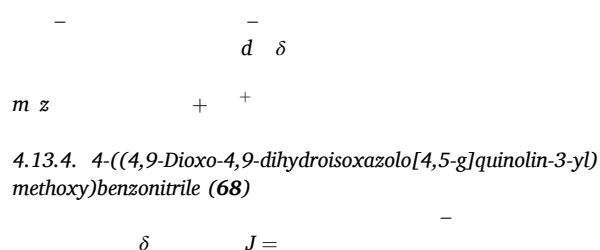
4.13.1. 3-(Phenoxymethyl) isoxazolo[4,5-*g*]quinoline-4,9-dione (**65**)



4.13.2. 3-((2-Chlorophenoxy)methyl)isoxazolo[4,5-*g*]quinoline-4,9-dione (**66**)



4.13.3. 3-((4-(Methylsulfonyl)phenoxy)methyl)isoxazolo[4,5-*g*]quinoline-4,9-dione (**67**)



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## Declaration of Competing Interest

## Acknowledgement

## References

